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SYMPOSIUM FOR THE GENERAL PRACTITIONER

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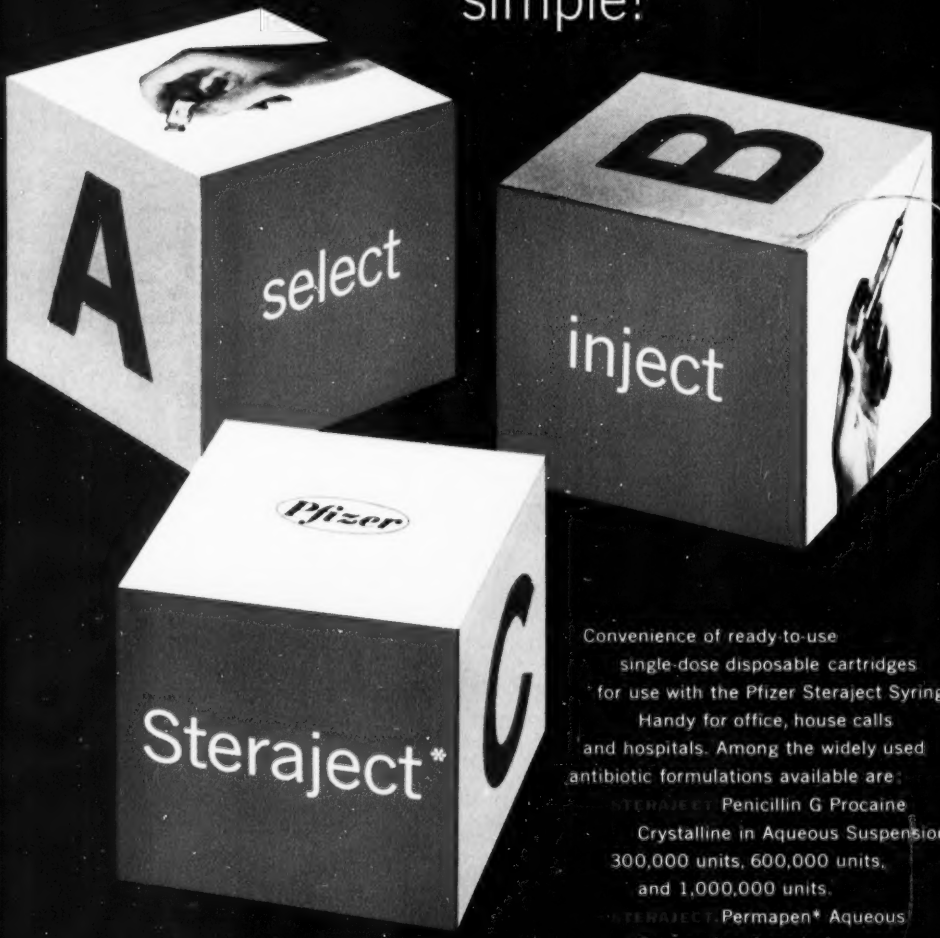

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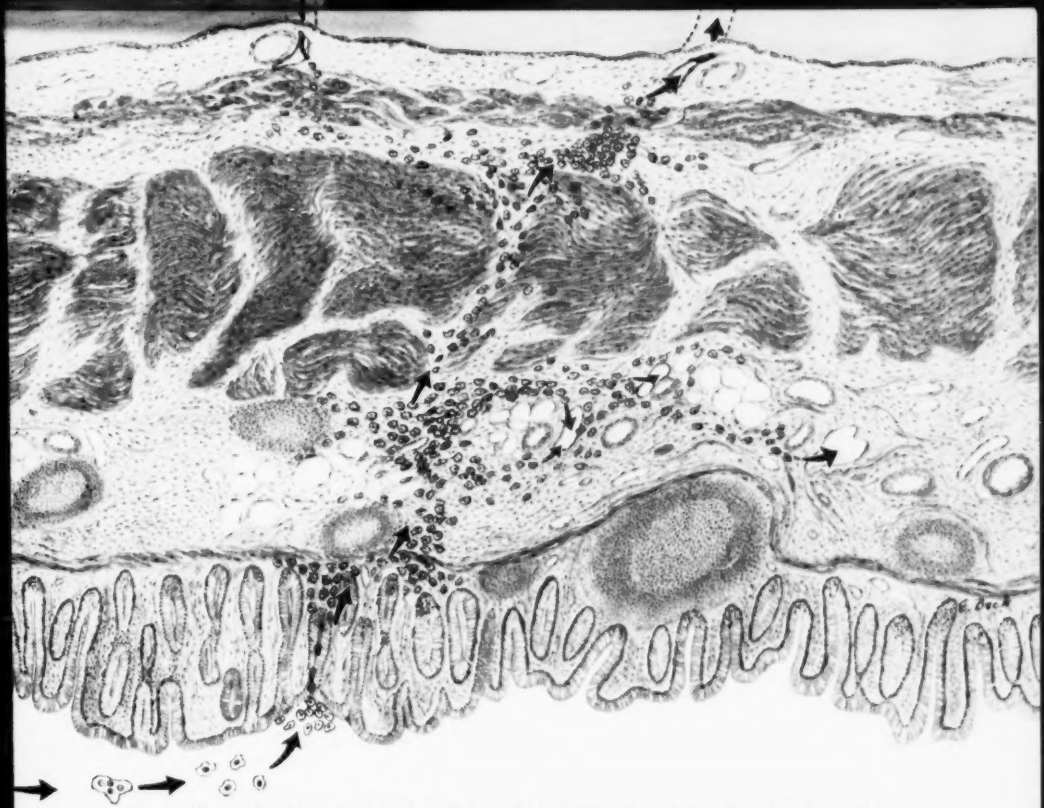

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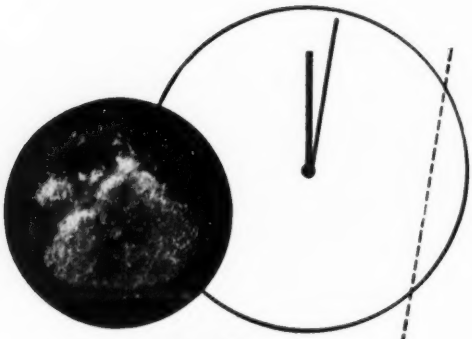

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THE Review of Gastroenterology

(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

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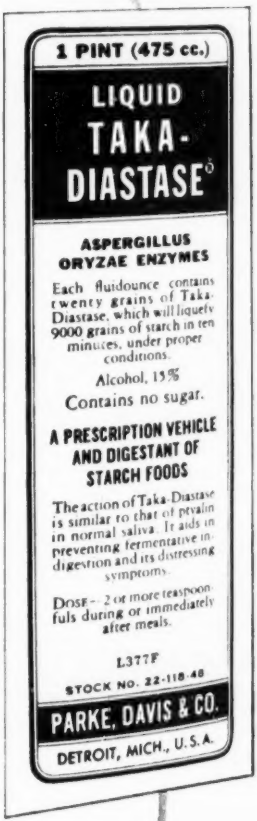

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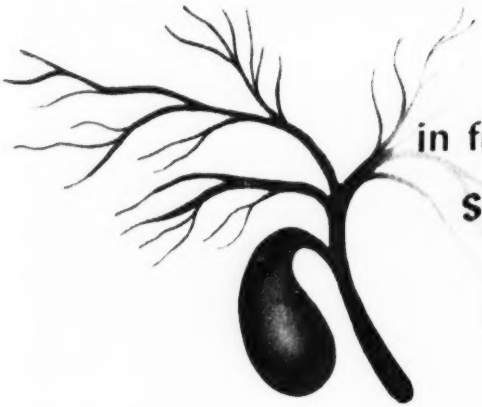

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SYMPOSIUM FOR THE GENERAL PRACTITIONER

ACUTE LOWER ABDOMINAL EMERGENCIES*

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INTRODUCTION

Surgery in acute conditions of the lower abdomen is an intriguing and fascinating subject that constantly challenges the skill and the ingenuity of the internist and the surgeon with its many complex problems. The slightest and perhaps, even the most trivial injury to the abdomen may prove serious and even disastrous. Quick thinking and sound judgment are of the utmost importance, as the mortality rate in most instances, is in direct proportion to delay.

That one must be constantly alert and of open mind when confronted by the problem of the acute surgical abdomen is emphasized by the fact that the syndrome may be simulated by uncommon medical entities, such as acute porphyria, as well as by the more common surgical emergencies, such as appendicitis. Table I demononstrates a legion of diseases that may present emergent surgical situations in the lower abdomen. For the purposes of this discussion the lower abdomen is arbitrarily described as that area of the abdomen below the level of the umbilicus. Table II demonstrates that the problem is not only that of the surgeon, but that there are many disease entities properly in the province of the internist that may be present in the acute surgical abdomen.

TYPHOID FEVER

In the not too distant past one of the prominent complications of typhoid fever was perforation of the small intestine or the cecum with extensive ulcera-

*Read before the Seventeenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 20, 21, 22 October 1952.

tion of the Peyer's patches. Subsequent to perforation a grave situation became worse with the picture of generalized peritonitis. Prompt diagnosis and the use of Chloramphenacol has virtually obviated this in the few cases that do occur.

Typhoid fever also occasionally presented the picture of the acute surgical abdomen when sudden hemorrhage would occur within the rectus sheath causing spasm of the rectus muscles which is difficult to differentiate from true peritoneal irritation.

The time allotted, of course, does not permit adequate discussion of this extensive group. With this in mind, I should like to confine my remarks to a few of these diseases in the light of our recent experience at The Roosevelt Hospital.

Acute Appendicitis

Acute appendicitis is one of the most common of abdominal conditions to be considered. The conventional triad of pain, nausea, and vomiting is well

TABLE I

Emergencies of the Lower Abdomen

1. Acute Appendicitis
2. Acute Diverticulitis
3. Intestinal Obstruction
4. Traumatic Injuries to Abdomen
5. Ruptured Corpus Hemorrhagicum
6. Acute Ulcerative Colitis
7. Ruptured Ectopic Preganancy
8. Torsion Ovarian Cyst
9. Acute Salpingitis
10. Endometriosis

known, and the results of early operation have produced a gratifying improvement in the mortality rate. There remain, however, a significant number of patients with acute appendicitis who have only anorexia, vague abdominal distress, minimal tenderness in the right lower quadrant and equivocal laboratory findings. This is particularly true of patients in the older age group. An elderly patient not infrequently harbors an advanced surgical pathologic condition within the abdomen with such a marked paucity of symptoms and signs that the true severity is not appreciated until too late, with consequent increase in the morbidity and mortality. These patients, too, warrant early surgical removal of the appendix and support the wisdom of early operation in those cases in which there is some question as to the diagnosis.

Diverticulitis

Diverticulitis is usually thought of as a disease amenable to medical management, however, at times it becomes a grave and immediate surgical problem.

It is true that a large percentage are successfully treated medically. A remarkably small number demand surgical intervention; for the most part it is the complications of the disease that necessitate surgery.

The most frequent complication is abscess formation with local peritonitis. This condition in the absence of obstruction requires incision and drainage alone. If obstruction is present decompression by means of cecostomy or more preferably by colostomy through an upper transverse incision is indicated.

Acute perforation of an inflamed diverticulum does occur and diffuse peritonitis ensues with rigid abdomen and diffuse tenderness. Many in this group are operated upon as emergencies with the diagnosis of acute suppurative appendicitis, acute salingitis, or perforated peptic ulcer. Many of the smaller perforations are immediately sealed off by the omentum or loops of small intes-

TABLE II

MEDICAL CONDITIONS SIMULATING THE SURGICAL ABDOMEN

1. Diabetes Mellitus
2. Uremia
3. Addison's Disease
4. Acute Congestive Failure
5. Coronary Thrombosis
6. Pericarditis
7. Dissecting Aneurism
8. Sickle-Cell Anemia
9. Leukemia
10. Henock's Purpura
11. Typhoid Fever
12. Measles
13. Porphyria
14. Pneumonia
15. Serum Sickness
16. Black Widow Spider Bite
17. Tabes Dorsalis
18. Herpes Zoster
19. Intercostal Neuralgia

tine or even by the fatty appendages of the descending or sigmoid colon. Some are sealed off by being fixed to the parietal peritoneum, or to the bladder. Of forty-four cases of perforations reported by the late Roscoe Graham, there were eleven cases or 25 per cent which presented as acute perforations and which necessitated emergency surgery. In our group, there was a preoperative diagnosis of acute diverticulitis with perforation made in eighteen instances. Many patients are operated upon through a McBurney incision because of the preoperative diagnosis of acute appendicitis. If the diagnosis is found to be erroneous, the intermuscular incision is closed and a larger incision offering greater exposure made—a left rectus incision. Occasionally, it seems justifiable to close a perforated diverticulum by putting a free graft or a pedicle on or to close the perforation with adjacent fatty appendages of the sigmoid colon. If this is done it would seem reasonable to do a proximal decompressing colostomy.

Acute Fulminating Ulcerative Colitis

In the acute fulminating stage of ulcerative colitis we are frequently confronted with the so-called acute surgical abdomen. These patients are desperately ill. The temperature is usually high, pulse rapid, weak and thready, and the blood pressure at low levels. The abdomen is tender to palpations particularly in the lower quadrants, there is muscular spasm, and peristalsis is active. The patients, too, are often "bled-out" and markedly debilitated by massive rectal hemorrhages. In our earlier experiences some fourteen years ago, we operated upon thirteen of these patients, giving them ileostomy with a mortality rate of 53 per cent. Needless to say, this was an untenable position. Because of this high mortality rate we insisted that our medical confreres rehabilitate these desperately ill patients up to the point where surgery would be safer. Within the last year we have operated upon six of these patients in the fulminating stage of the disease, resecting their colons and giving them ileostomies in one stage. We have felt justified in carrying out such a radical procedure, for it was the only means of controlling the threat of hemorrhage and the extreme "toxicity" presented. Large

TABLE III

Types of Trauma

Automobile Accidents	3
Blunt Blows (Wood, Pipe, Fist)	3
Falls	1
Crush	1
Handles	1

amounts of blood have been necessary in the preoperative period and have been a significant factor in the success of these emergency procedures.

In a small percentage of patients suffering from the chronic form of the disease, perforation of the bowel has taken place and has produced a peritonitis with the typical signs of the acute abdomen.

Intestinal Obstruction

There are many etiological backgrounds for obstruction of the colon and of the small intestine; however, if one should survey any large series of cases of obstruction the incidence of strangulated external hernia will rank near the top. As a rule 45 to 50 per cent of cases of obstruction will be secondary to strangulated hernia. This is in contrast to postoperative adhesions which are at fault in 20 to 25 per cent; and neoplasm which accounts for 10 to 15 per cent.

External orifices in the lower abdomen at which hernia occurs most frequently are the inguinal, femoral and umbilical. These are also the herniae that most frequently give rise to intestinal obstruction and symptoms of strangulation. Strangulated hernia is essentially a disease of active adult life, most cases occurring between the ages of twenty and fifty, although it may obtain from infancy up through old age.

In inguinal hernia the external ring constitutes the most frequent cause of strangulation. Less frequently, strangulation occurs at the internal ring; and occasionally the constriction may be in the sac. Right inguinal hernia is more frequent than left, and similarly strangulation on the right side is observed more frequently than on the left. Because of the more gradual development of direct inguinal hernia and the progressive stretching of the hernial orifice strangulation only infrequently occurs in direct hernia. Femoral hernia ranks as one of the common causes of intestinal obstruction of the strangulating variety. Femoral hernia is much less common than inguinal, still the frequency with which strangulation occurs in femoral hernia closely approximates that of the inguinal group. The rigid wall formed by Pouparts', Gimbernat's, and Cooper's ligaments constitute a treacherous aperture through which a loop of bowel may protrude. In consonance with the greater incidence of femoral hernia in women, strangulation also occurs more frequently in the female. The rigid fascial insertions into the linea alba at the umbilicus make for frequent strangulation of the intestine at this site.

Mechanical obstruction of the intestinal tract whether it be due to hernia, simple postoperative adhesions, or volvulus of the sigmoid colon presents two

TABLE IV

Ruptured Ectopic Pregnancy

Roosevelt Hospital 1940-1951	57 Patients
Accurate Preoperative Diagnosis	91.0%
Whole Blood Transfusions	52 Patients
Total Amount Whole Blood	61,000 c.c.
Death Congestive Heart Failure Following Surgery	1 Patient

immediate problems: decompression of the proximal bowel and removal of the causative agent. The first problem is imperative and may be accomplished by means of the Miller-Abbott tube or comparable tube or upon the operating table. The second is of much less immediate importance and may be dealt with when the condition of the patient warrants it. The Miller-Abbott has been a very useful adjuvant, but it is pertinent to note that no delay should be tolerated in procrastination over whether or not the Miller-Abbott tube will be effective.

Traumatic Injuries to the Abdomen

Gunshot wounds, stab wounds, fractures of the pelvis with laceration of the urinary bladder usually present a straight-forward picture on entry into the hospital. It is possible, however, to have laceration of the small intestine secondary to nonpenetrating trauma of the abdominal parietes. It is an unusual lesion but one that is apt to result in disaster if not diagnosed early or operated upon promptly. The type of violence necessary to cause the laceration of the small intestine varies widely, but in most cases is the result of a severe, sudden blow with a blunt object when the patient is not expecting it. Auto accidents ranked

first on our list with the trauma occurring on sudden acceleration with the patient thrown against the steering wheel or against the back of the front seat, or struck by a fender. Handles, kicks, crushing injuries, blunt blows, and falls, however, may be responsible. It is important to remember that trauma may have been insignificant enough to have been forgotten. One of our patients struck himself in the abdomen when his hand slipped opening a bottle of champagne. Table III illustrates the types of trauma encountered in our series. Kicks and attempts to reduce incarcerated hernias have also resulted in perforation.

The clinical sequence following perforation in most cases is that of a rapidly developing peritonitis with sudden local pain succeeded by generalized severe prostrating abdominal pain with or without nausea or vomiting. The abdomen is tender generally with marked muscle spasm, absent peristalsis, and in 1/3 of cases absent liver dullness. In three of seven instances where the examination was carried out three-way films of the abdomen—40 per cent demonstrated free air in the peritoneal cavity.

In two instances in this series, however, the initial trauma had been forgotten, there was only "soreness" in the abdominal wall, there was no other associated symptomatology and the physical findings revealed only minimal tenderness in the area of concern without spasm of the muscles. Peristalsis was present, there was liver dullness, and three-way films of the abdomen were negative for free air. These two patients demonstrated so little that they were discharged from the Accident Room only to return 6 to 12 hours later with the complete picture described above. These patients were not perforated at the initial examination and were found at operation to have had mesenteric lacerations and laceration of the small intestine adjacent to the mesenteric attachment. It was felt that initially there was compromise of the blood supply of the involved portion of the small intestine severely traumatized at the initial injury, although the continuity remained.

Early operative intervention is necessary in these cases for if repair is carried out soon enough, less than 12 hours, the opportunity for survival is improved. When no operation is carried out the outcome in each case is death. If the operation were carried out before 12 hours had elapsed, the operative mortality would have been 19 per cent as opposed to that carried out after 12 hours when the operative mortality was 35 per cent. The mortality rate is too high and in part is due to the fact that the possibility of perforation having been suspected is disregarded when the roentgen studies fail to show free air under the diaphragm. Too much time is spent in wishful observation. If there is persistent abdominal pain, tenderness, with or without nausea or vomiting subsequent to severe or even minor trauma to the abdomen and these persist for six hours, exploratory celiotomy should be carried out. Under these circumstances reasonable suspicion, as in acute appendicitis not only justifies, but demands immediate surgery. The dangers of delay are far greater than the hazards of surgery.

In considering emergency situations of the lower abdomen *in female patients,* one not frequently encounters disease entities involving the pelvic organs of reproduction.

Ruptured Ectopic Pregnancy

The classical picture of a ruptured tubal pregnancy is a paramount surgical emergency. Prior to 1900, it was considered as a catastrophe that was without parallel. Subsequent to 1900 until the ready availability of whole blood, a mortality of from 4 to 8 per cent was expected.

In the Roosevelt Hospital during the past decade (1940-1951), fifty-seven cases of proved ruptured tubal pregnancy have been operated upon (Table I). An accurate diagnosis, based on the cardinal manifestations of a ruptured extrauterine pregnancy, i.e., pain, bleeding, amenorrhea, and the presence of a pelvic mass, was made prior to surgery in 52 cases or 91 per cent of all cases seen. In four patients, the abdomen was opened with a preoperative diagnosis of acute appendicitis and in one instance, the patient was believed to have a ruptured ovarian cyst. Nineteen patients or 33.3 per cent of all patients seen were stated

TABLE V

Ruptured Hemorrhagic Ovarian Cyst
(Follicular, Luteal, Endometrial)

In past 10 years	52 surgical emergencies
Preoperative diagnosis appendicitis	40 patients
Right ovary site of rupture	48 of the 52 patients

to have been in shock on or soon after admission. Fifty-two patients received whole blood transfusions and during the ten years surveyed, it was found that a total of 61,000 c.c. of whole blood were administered to patients with proved ruptured tubal pregnancies, an average of 1,000 c.c. being administered to each of the 57 patients. Only one patient died and she expired in congestive heart failure following surgery.

It is apparent that the best treatment of this illness is surgical as soon as the diagnosis is established and as soon as the condition of the patient permits it. The generous use of whole blood transfusions cannot be too highly endorsed for the critically ill patient. Measures to combat collapse should be promptly instituted and the patient should be moved to the operating room as soon as it is feasible.

The type of incision employed probably is unimportant but we generally favor a suprapubic midline incision. We believe that only the required surgery should be done, it being unwise to perform elective surgery, particularly if there has been much blood loss. We attempt to remove the extravasated blood but autotransfusions are believed to be contraindicated because of the rapid hemoly-

sis of blood that takes place in the peritoneal cavity and the high percentage of bacterial contamination in blood removed from the abdomen.

Having established an early diagnosis, prompt surgery, supported by better anesthesia, and the liberal use of whole blood transfusions, should reduce the mortality of this illness in 1952 to less than 1 per cent.

Ruptured Hemorrhagic Ovarian Cysts

Female patients with right lower abdominal pain (frequently associated with nausea, vomiting, slight elevation of temperature and a moderate leucocytosis) are often believed to have acute appendicitis but at surgery are found to have ruptured hemorrhagic ovarian cysts, the latter terminology being used to include all hemorrhagic cysts, whether follicular, luteal, or endometrial. This disease entity was noted 52 times in our survey of surgical emergencies operated upon during the past ten years (Table V). In 40 of these patients, the preoperative diagnosis was acute appendicitis. Only six patients were believed to have an ovarian cyst and five were thought to have an ectopic pregnancy. Needless to say, the right ovary was the more frequent offender, it being the site of rupture in 48 *of the* 52 *cases.* In two instances, there had been sufficient hemorrhage to warrant transfusions, one patient having received 1,000 c.c. of whole blood during and following the operative procedure. In no instance was the patient in shock, but all patients were considered as emergencies.

TABLE VI

Torsion of ovarian cysts (10 year period)	18 patients
Preoperative diagnosis correct only in	4 patients
Youngest patient	8 years
Oldest patient	80 years

Torsion of Ovarian Cysts

Patients with ovarian cysts in whom there had occurred torsion of the ovarian pedicles, have been encountered somewhat less frequently, only eighteen patients having been operated upon and the diagnosis substantiated at the time of the operative procedure during the past ten years (Table VI). These patients not infrequently related a history of recurrent episodes of lower abdominal discomfort associated with nausea and vomiting, although the onset of pain prior to surgery usually was sudden and severe. In only eight cases or 44.4 per cent of all cases seen, was the diagnosis entertained prior to surgery. Six patients were believed to have had acute appendicitis. There was no predilection for any age group. The youngest patient operated upon was eight years of age and the oldest was 80. One patient was pregnant. No malignant tumors were encountered. Six cysts were found to be dermoids, nine were described as simple cysts, two were corpus luteum cysts, and one was a paraovarian cyst.

Torsion of ovarian pedicles undoubtedly occurs more frequently than our statistics would indicate, the patients presenting themselves only when there

has been sufficient embarrassment to the circulation of the structure to produce persistent symptomatology. *Nevertheless,* the possibility of a ruptured hemorrhagic ovarian cyst or torsion of an ovarian pedicle must be entertained in any female patient with acute lower abdominal pain.

If the appendix has been removed and one cannot palpate a pelvic tumor, in the absence of a history suggesting a ruptured ectopic pregnancy, one can frequently judiciously observe the patient for a reasonable period of time to *better establish the diagnosis;* however, where there is doubt, an immediate exploratory celiotomy should be performed through an adequate incision even if the suspected diagnosis is that of a ruptured hemorrhagic ovarian cyst. Simple resection or excision of the cyst can be accomplished without difficulty, *every effort being made to conserve ovarian tissue.*

Acute Salpingitis

The problem presented to the surgeon by a patient with acute salpingitis is less frequently encountered today than previously, but it still remains an interesting and important one. Many of these patients are seen in the emergency units of our city hospitals and are treated on a semiambulatory basis once the diagnosis is established.

TABLE VII

Acute Salpingitis

If diagnosis is *definitely* established *Surgery not Indicated*
If however there is evidence of progressive or ascending peritonitis, prompt surgical intervention mandatory. Drainage through posterior colpotomy.

The most important differential diagnosis to be ruled out is that of acute appendicitis but if one takes a detailed history referable to the onset of the illness and its course, together with a careful abdominal and pelvic examination, the diagnosis is not usually difficult to establish. At times, however, it is impossible to distinguish the findings in a patient with acute salpingitis from those one might expect with acute appendicitis, torsion of an ovarian pedicle, rupture of a hemorrhagic ovarian cyst, or even a ruptured ectopic pregnancy. If this is the case, one should operate immediately because of the danger of neglecting the patient with a "surgical" abdomen which demands intervention. If at the time of surgery, the patient is found to have an acute salpingitis or an exacerbation of a chronic process, it is not necessary to remove the tubes unless one is fairly certain that they will cause further trouble. If the patient is a young woman, it would seem far wiser to give her the benefit of a chance to have a normal reproductive life. Today, with penicillin, the sulfonamides, and the broad spectrum antibiotics, these patients usually respond remarkably well. If the diagnosis is definitely established, surgery is not indicated, for the pelvic structures are usually capable of localizing and overcoming the infections by their inflammatory reac-

tion, aided and abetted by chemotherapy (Table VII). In certain instances, where the pelvic reaction can halt the progress of the infection, but forms abscesses, or cannot halt the infection, allowing generalized peritonitis to develop, then surgery may be necessary. In these situations where there is evidence of a progressive or ascending peritonitis, *prompt surgical intervention may be mandatory*, drainage being established through a *posterior colpotomy wound*, or if warranted, by laparotomy.

Endometriosis with Acute or Subacute Obstruction of the Small or Large Bowel

Occasionally, one sees a patient presenting herself as an emergency, with less frequently encountered disease entities related to the pelvic viscera. These include the pedunculated myomata with twisted pedicles, the degenerating myomata, ruptured, nonhemorrhagic ovarian cysts, and even torsion of the Fallopian tubes. Endometrial implants on the large and small bowel can cause partial or

TABLE VIII

Endometriosis With Acute or Subacute Obstruction Of the Small or Large Bowel

7 Patients

5 Partial obstruction
2 Complete obstruction
3 Endometrial lesions involving the terminal ileum
4 Resection of endometrial lesions end-to-end anastomosis of bowel

complete intestinal obstruction (Table VIII). This interesting situation has been encountered on our surgical service seven times during the past ten years, obstruction being partial in five instances and complete in two. The lesions involved the rectosigmoid colon in four patients, two of whom had complete obstruction. In three instances, the endometrial lesions involved the terminal ileum. One patient, who had had a previous end-to-end anastomosis for severe chronic ulcerative colitis, subsequently developed obstruction due to an endometrial lesion at the anastomotic site. A colostomy was performed. In another patient with complete obstruction due to endometriosis involving the rectosigmoid colon, gratifying relief was obtained after an abdominal hysterectomy and a bilateral salpingo-oophorectomy. Four patients had resections of the endometrial lesion with end-to-end anastomoses of the bowel and two of these also had an abdominal hysterectomy with bilateral salpingo-oophorectomies. In no instance, to our knowledge, has there been a recurrence of obstruction in any of these patients.

Conclusion

When in the slightest doubt as to the nature of any low abdominal emergency—open the abdomen.

INSULIN AND DIABETES
ENDOGENOUS AND EXOGENOUS INSULIN

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Diabetes, today, is generally defined as a condition resulting from an absolute or a relative deficiency of insulin. Every case of diabetes may be managed and possibly completely controlled by suitable amounts and kinds of insulin, or by dietary restrictions without the aid of insulin, or a combination of both. The diabetic, however, is subject to certain complications: arteriosclerosis of the lower extremities, coronary thrombosis, retinopathy and nephritis. The prevention of the occurrence of these has not been solved and they may result in invalidism or premature death. It is hoped that a contribution in this direction may be made by analyzing the difference of the effects of the body's own insulin, endogenous insulin, and that given by injection, exogenous insulin.

Postprandial Blood Sugar

An analysis of blood sugar in nondiabetics up to 4 hours after lunch showed that the postprandial blood sugar was not above the accepted normal range of the fasting state (Fig. 1). This finding has been verified by observations of Ackerman and Bohan (1951)[1] in after-breakfast blood sugar in normals. It must, however, be recognized that while this applies to the blood sugar determined one and two hours after eating, a distinct rise of blood sugar usually occurs ½ hour after meals. A considerable rise of blood sugar usually occurs after lunch in diabetics, receiving insulin, who have a normal blood sugar preceding the meal (Fig. 2). The same findings, except that the observations were made after breakfast, have been recorded by Ricketts (1938)[2]. It thus becomes apparent that both for the diagnosis of diabetes as well as for guidance in the regulation of diabetes, a postprandial determination of blood sugar is preferable to the usual estimation in the fasting state, which puts an unnecessary burden upon the patient, the physician and the technician.

The postprandial rise of blood sugar can often be controlled by diminishing the carbohydrate content of the diet. In one of Ricketts' cases there was virtually no rise in blood sugar after a breakfast containing 19 grams of carbohydrate though considerable hyperglycemia ensued after the taking of 25 or 31 or 39 grams of carbohydrate. Thus the eating of 19 grams of carbohydrate was handled by this diabetic in a physiological manner, but a greater amount could not be cared for in this way.

All of these facts point to the conclusion that, if the basic secretion of insulin is sufficient, the liver is able to dispose of or assimilate all the glucose

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ingested at each meal, there is no postprandial rise of blood sugar and no additional insulin will be required. If a postprandial rise of blood sugar occurs, the need for extra insulin secretion becomes evident. In normals this is found ½ hour after eating but does not persist for 1 hour after eating.

Endogenous and Exogenous Insulin

The insulin secreted by the pancreas may be termed endogenous insulin and the insulin administered by hypodermic injection, exogenous insulin. The endogenous insulin is carried in the portal vein from the pancreas to the liver where it makes an exclusive primary contact with tissue, excepting the blood in the portal system. Exogenous insulin, whether given subcutaneously or by vein, passes to the whole body, the muscles, skin, heart, kidneys and other organs, but according to the anatomy of the arteries only a comparatively small amount

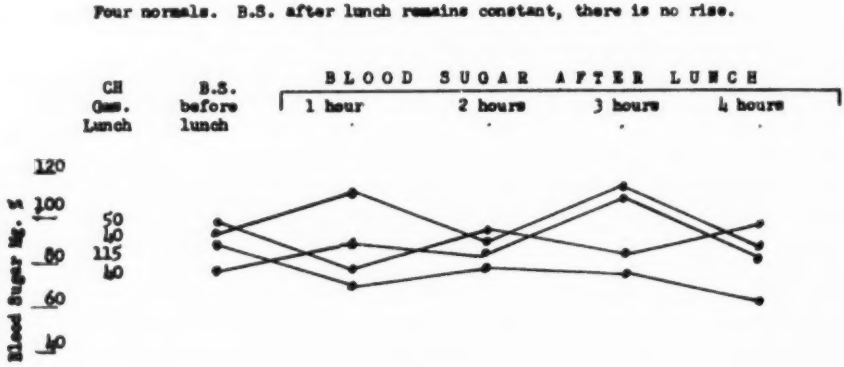

Fig. 1

reaches the liver. Recent researches have indicated that a difference exists between the effect of endogenous and exogenous insulin. Insulin, according to the *in vitro* experiments of Stadie et al (1949)[3], makes a stable combination with muscle tissue it contacts though it still retains its power to metabolize glucose. Under normal conditions, insulin secreted by the pancreas passes through the portal vein to the liver where it has its first impact on tissue and subsequently the insulin not bound by the liver enters the general circulation where its continual presence has been demonstrated. A lack of insulin in the blood stream may be completely substituted for by injected, exogenous insulin, but a deficit of insulin in the portal vein, because of diminished pancreatic activity, will not be completely replaced by injected, exogenous insulin.

The dominance of the insulin effect in the immediate locality which it supplies, is shown in the observations of Bell and Burns (1952)[4]. They found that when small amounts of insulin were injected into one femoral artery the arterio-

venous blood sugar difference was much greater in the injected leg than in the opposite leg. The injection of the same amount of insulin into the antecubital vein, however, resulted in similar effects in both legs, thus making it certain that the intensity of response of the peripheral tissues to insulin is in direct proportion to the amount of insulin they come in contact with and that they bind at least a

TABLE I

EFFECTS OF REGULAR INSULIN ON FASTING VENOUS BLOOD SUGAR

Case	Regular Insulin Units	Blood Sugar mg. Per Cent								Duration Hours Drop B.S.
		Before Insulin	After Insulin							
			1 hr.	2 hrs.	3 hrs.	4 hrs.	5 hrs.	6 hrs.	8 hrs.	
1	20	428	386	186	119	133				3
2	15	377	357	303	175	103				4+
3	20	353	349	234	151	141				4+
4	30	342		197		180		131	104	8
5	10	341	331	199	181	165				4+
6	20	319		250		197		208	221	4
7	20	312	314	272	263	230				4+
8	23	308	256	220	180	150	172	190		4
9	20	291	248	146	100	70				4+
10	20	263	233	193	180	153				4+
11	15	260		192		166		187	192	4
12	20	248	163	52	84	89				2
13	20	211	167	142	117	120				3
14	5	200		110		86		91	101	4
15	10	190			114	80	79			5+
16	20	190	160	122	92	86	83			5+
17	20	179	163	100	81	62				4+
18	20	176	100	78	87	95	103			2
19	10	156			90	77	85			4
20	20	146	120	86	76	75	85			4
21	20	128	74	60	66	76				2
22	15	109	72	65	69	67				2
23	20	100	75	45	51	55				2
24	10	91			57	52	52			4
25	15	83	71	58	58	58				2
26	20	79	60	60	60	65	62			1
27	20	78	44	58	56	59	58			1

Doses of 5 to 20 units of unmodified insulin reduce the fasting B.S. to normal regardless of the level of the fasting B.S. which varied from 78 to 428. None of the subjects had any insulin with prolonged action on the preceding day. This points to the great power of self-regulation, homeostasis, of the blood sugar inherent in normals and diabetics.

part of the insulin. The action of this bound insulin is limited to the immediately adjacent tissue.

The endogenous insulin, the body's own insulin, secreted into the portal vein, would, according to these concepts, have its principal effect upon the liver, whereas the exogenous, the injected insulin, would influence mainly the extrahepatic tissues. Diabetes controlled by injections of insulin may be regarded as

having satisfactory regulation of the extrahepatic carbohydrate metabolism but not necessarily of that in the liver. The finding of Richardson (1933 to 1942)[5] that the glycogen content of the liver is more important for the prevention of infection than the control of hyperglycemia or of other changes, points to the inherent deficiency of our present treatment of diabetes, which may possibly be a cause for the unexplained tendency to the development of retinopathy, nephritis and arteriosclerosis. The sequence of events in the pathological physiology of diabetes is somewhat as follows: lack of insulin, rise of blood sugar, glyco-

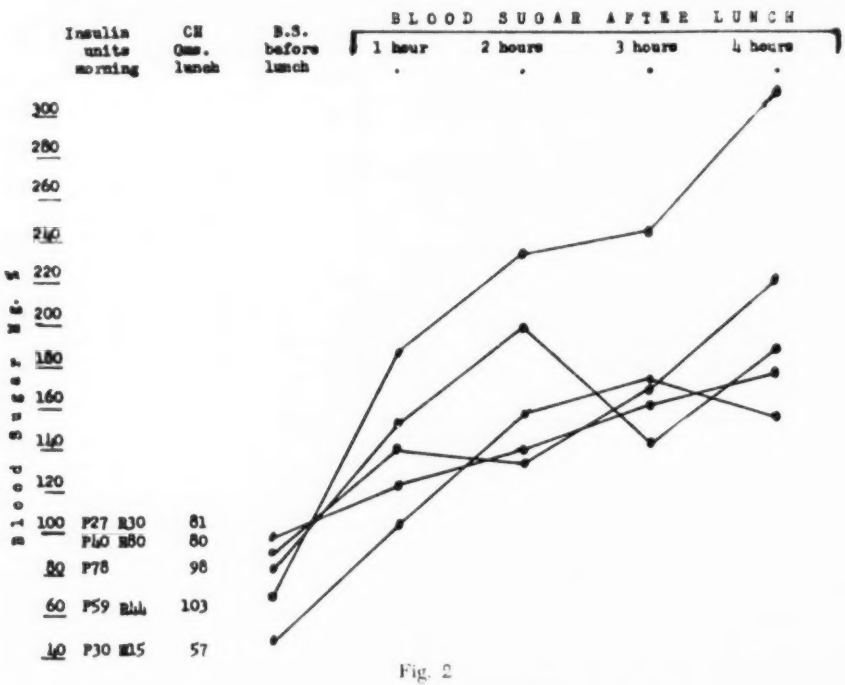

Fig. 2

suria, polyuria, depletion liver glycogen, dessication, protein destruction, marked diminution of glucose combustion, acidosis.

The point at which it is known that bodily damage arises is when the glycosuria becomes excessive and the consequences occur as just detailed. An elevated blood sugar in itself without distinct, persistent glycosuria is probably a harmless condition (Mosenthal, 1935)[6]. It is difficult to say what part depletion of liver glycogen, dessication and protein destruction play in putting the diabetic out of

commission, but it would seem that all three are major influences in bringing about the deteriorations characteristic of diabetes. The depletion of liver glycogen, however, may set in before the other vital factors mentioned become important, as expressed in the scheme above, and thus would be the earliest to occur following inordinate glycosuria and polyuria.

Basic and Extra Insulin Secretion by the Pancreas; An Interpretation of the Action of Endogenous Insulin

In the preceding section a differentiation was made between endogenous and exogenous insulin. The latter is the insulin administered by injection, the former

TABLE II

PZ Insulin Administered Every Other Day Controls Some Diabetics

Date	Urine Glucose %	Blood Sugar* Mg. %	PZ Units Every Other Day	Remarks
Mar '35	Trace	125	0	Diet throughout C 134 or less P 104 F 123
May '36	2.6	296	0	Frequent dietary transgressions
May '39	0.4	213	0	All blood sugars obtained after breakfast
Oct '39	0.0	182	24	No hypoglycemic reactions at any time
Nov '40	0.0	160	28	Insulin dosage always geared to basic diet;
May '41	Trace	186	46	adjustment for dietary transgressions not
Sep '42	0.0	133	80	attempted.
Jul '43	0.0	100	76	
Mar '44	0.0	130	70	
May '45	0.0	155	70	Cholecystectomy gallstones
Oct '46	0.0	145	74	
Sep '47	0.0	120	80	Hydrocele operation
Aug '48	0.0	167	86	
Aug '49	0.2	167	86	
Jun '50	0.0	139	86	Renal calculus, not operated—fewer visits
Jan '51	0.0	220	86	overconfident about diabetes
May '52	0.0	218	86	Eyes normal for age

J. U., male, onset diabetes in 1934, at age 38. Diabetes at first controlled by diet only; later insulin became necessary; glycosuria successfully regulated by insulin injections every other day. This case shows that when PZ insulin is adjusted to a low basic CH diet and not changed when there are indications for an increase of insulin dosage because of extra CH eaten, that there will be no hypoglycemia and that the diabetes can be completely regulated by the ability of the liver to care for the slow absorption of CH without throwing an extraordinary burden upon the peripheral tissues.

*B.S. after breakfast

is the insulin secreted by the pancreas. Endogenous insulin derived from the pancreas, may be further subdivided into two varieties according to the stimulus which acts upon the pancreas. One is the basic insulin constantly secreted and the second is the extra insulin put out by the pancreas in response to a rise of blood sugar in the pancreatic artery; hyperglycemia in the portal vein does not augment insulin secretion (Houssay, Lewis and Foglia, LaBarre)[7].

The basic insulin from the pancreas is sufficient to prevent a postprandial rise of blood sugar in normals (Fig. 1), and without hyperglycemia there is no stimulus for extra insulin secretion. This effect of basic insulin may be explained on two grounds. In the first place there is the probability of a considerable storage of insulin in the liver as previously discussed; secondly the enormous flexibility of the power of insulin to keep the blood sugar at a normal level without the production of hypoglycemia deserves consideration. In Table I the blood sugar is maintained at normal levels by the injection of 20 units of unmodified insulin whether the fasting blood sugar be as high as 428 mg. per cent or as low as 78 mg. per cent. According to the insulin requirement of 30 to 40 units per day

TABLE III

HYPERGLYCEMIA IS NO OBSTACLE TO RESUMPTION OF NORMAL B.S. WHEN URINE IS KEPT SUGAR-FREE WITHOUT USE OF INSULIN*

Date	Urine Sugar %	Blood Sugar** Mg. %	Diet
1952	Glycosuria for preceding 17 months		
May 29	2.0	225	Free diet including sugar
Jun 2	0.0	289	About 75 gms. CH
10	1.0	237	" 75 " CH
19	0.9	183	" 75 " CH
27	0.2	295	" 75 " CH
Jul 10	0.0	221	" 75 " CH
25	0.3		" 75 " CH
Aug 1	0.0	201	" 90 " CH
20	0.0		" 90 " CH
28	0.0	130	" 90 " CH
Sep 25	0.0	80	" 90 " CH

Mrs. R. H. M., age 53. Glycosuria for 17 months. No improvement while taking a free diet. With elimination of sugar and sugar containing foods, the strict limitation of carbohydrates and the enthusiastic cooperation of the patient, the urine became sugar free, or almost so; hyperglycemia continued for 3 months and then became normal. This study shows beautifully how tolerance may improve while the blood sugar is high provided glycosuria is controlled. Without the latter there was no improvement during 17 months.

*ambulatory treatment **B.S. determined after breakfast

in pancreatectomized man, 20 units must be regarded as a large dose. In Table I the results are shown to be equally good with smaller amounts of insulin, even as little as 5 units.

These facts explain the observation of Soskin, Allweiss and Cohn (1934)[8] when they infused pancreatectomized dogs with constant amounts of insulin and found a normal disposition of additional glucose.

There is always some insulin in the peripheral circulation of normals. When a sufficient quantity of sugar is ingested a hyperglycemia results and this causes a secretion of extra insulin. Recently Bornstein (1950)[9], by perfecting the quanti-

tative estimation of insulin in the blood, has shown that after the taking of glucose by normal individuals the amount of insulin in the circulating blood rises. The following is quoted from a review of his work:

"Under the conditions of the experiment the plasma insulin concentrations were 0.1 milliunit/ml. during fasting and 0.2 milliunit/ml. 1 hour after, 0.34 milliunit/ml. 2½ hours after and 0.22 milliunit/ml. 3½ hours after ingesting of glucose. Plasma insulin concentration increases as the blood sugar rises, reaching a maximum 1 hour after the peak of the blood sugar curve and thereafter declining. The further fall in blood sugar which then occurs and which is often seen

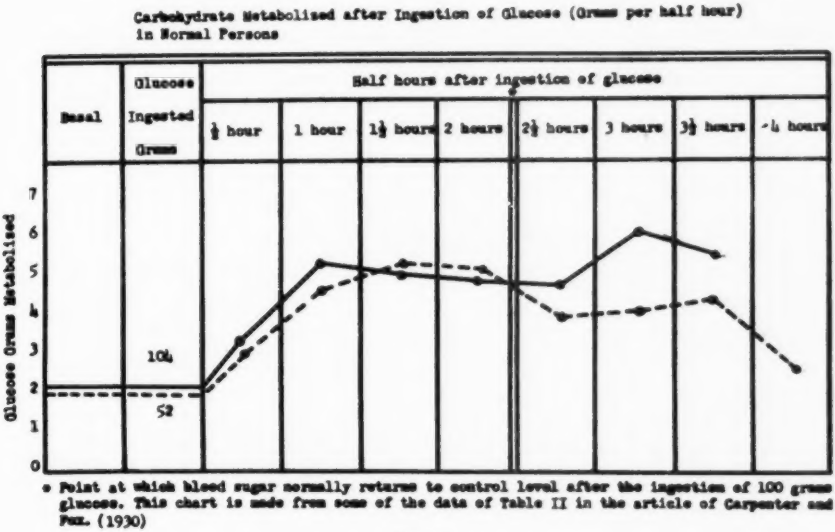

Fig. 3

in standard blood sugar curves, is considered due to excess insulin present after blood sugar has returned to normal."

This furnishes an explanation for the long debated question as to the development of a subnormal level of blood sugar found in the third and fourth hours of a glucose tolerance test. These observations also show that the entire increment of insulin is not retained in the liver, but that some of the endogenous insulin passes through the liver into the general circulation. In these experiments the blood insulin reaches its height 2½ hours after the ingestion of glucose and at 3½ hours is still more than twice the control value. This confirms the observations of Carpenter and Fox[10] (Fig. 3) that the amount of glucose metabolized continues at double the normal level 4 hours after the ingestion of 100 grams of glucose, that is for 2 hours after the blood sugar returns to normal.

It is evident that in diabetes the amount of basic insulin in the blood stream may be fully replaced, but the quantity passing to the liver through the portal vein must necessarily be deficient. As compensation for such a lack of adaptation of injected insulin recourse may be had to very low starch diets, so low that a postprandial increase of blood sugar will not occur. The proteins which supply the needed sugar under these circumstances release glucose very slowly and over a long period which makes it possible for the liver to assimilate all the glucose and prevent a postprandial hyperglycemia. This would appear to be the most efficient way of bringing about a normal glycogen content of the liver and preventing glycosuria, polyuria, dessication and protein destruction.

TABLE IV

HYPERGLYCEMIA IS NO OBSTACLE TO RESUMPTION OF NORMAL B.S. WHEN URINE IS KEPT SUGAR-FREE WITHOUT USE OF INSULIN*

Date	Urine Sugar %	Blood Sugar** Mg. %	Diet
1951	Glycosuria for preceding 6 months		
Apr 11	2.8	497	About 130 grams CH
27	0.3	269	" 25 " CH
30	0.1	210	" 25 " CH
May 8	0.0	149	" 25 " CH
Jun 14	0.0	144	" 40 " CH
Jul 6	0.0	127	" 55 " CH
1952			
Jan 18	0.0	117	" 85 " CH
Mar 21	0.0	124	" 85 " CH
May 29	0.0	127	" 85 " CH

A. A. G., male, age 60. Glycosuria for 6 months. No improvement while taking a low starch diet. With extreme restriction of starches the urine became sugar-free and the fasting B.S. was almost normal within 4 months and remained so for 10 months. This study shows very well how tolerance may improve while the B.S. is high provided glycosuria is controlled. Without the latter there was no improvement during 6 months.

*ambulatory treatment **B.S. after breakfast

Protamine zinc insulin comes closer to replacing the basic insulin secretion than any of the other insulins and with the aid of low carbohydrate diets it usually suffices to regulate almost any diabetic. When given in large doses it acts for a very long period. A recent report showed that a diabetic taking 2,000 units of protamine zinc insulin with suicidal intent suffered from hypoglycemic reactions for six days (Vogl and Youngwirth 1949)[11]. Such results, of course, should be avoided but the fact that apparently constant liberation of insulin takes place from protamine zinc insulin for several days may be taken advantage of by the injection of this insulin every other day instead of every day (Table II).

Management of Diabetes for Ideal Results

The diet should be sufficiently low in carbohydrates to prevent a postprandial rise in blood sugar. Under these circumstances, where no insulin is required, the ideal of a normal utilization of glucose is realized. This duplicates the adequacy of basic insulin secretion in the nondiabetic. It is appreciated that with a low carbohydrate intake the glucose tolerance assumes diabetic characteristics. This is found in normals with a daily intake of 50 grams of starch or less and disappears when 125 grams or more are taken; what the actual limits of carbohydrate intake are for attainment of a normal glucose tolerance has not been ascertained. All that is known is that habitual ingestion of more than 50 grams of starchy food and probably less than 125 are required for the glucose tolerance test to assume a normal picture (Himsworth 1935)[12].

TABLE V

Some Diabetics Improve While Receiving Insulin**

Date	Urinary Glucose %	Blood Sugar* Mg. %	PZ Insulin Units	Diet and Remarks
Apr 8 '41	2.0	313	0	CH 150 gm. throughout
May 9 '41	0.1	143	58	No hypoglycemia reactions
Jul 2 '41	0.0	129	30	No change in weight
Nov 11 '41	0.0	127	10	
Feb 7 '42	0.0	125	5	15 lbs. overweight for
Dec 7 '43	0.0	113	0	height and age.
Jul 11 '44	0.0	118	0	
Jun 28 '45	0.0	172	0	
Nov 20 '47	0.0	85	0	
May 8 '48	0.0	122	0	
Apr 9 '49	0.0	105	0	

U. J. S. male, age 50 in 1941. Glycosuria for 2 months preceding April 8, 1941. From a dose of 58 PZ, the insulin was omitted entirely in two year's time and sugar did not recur in the urine for a period of 7 years.
*B.S. taken after breakfast **ambulatory treatment

It should, however, be borne in mind that while a diminished glucose tolerance test serves a purpose as a diagnostic measure of diabetes, an impaired glucose tolerance is not necessarily incompatible with a normal existence, full enjoyment of health and even considerable intake of starch without the production of glycosuria.

On very low starch diets, without any insulin, many diabetics will have a remission of their diabetes even though they have exhibited a glycosuria for some months previously. Hyperglycemia does not prevent a partial rehabilitation of the pancreatic function for the production of insulin (Tables III and IV).

When insulin becomes necessary for the control of diabetes it would seem, for the reasons already given, that protamine zinc insulin replaces the basic

secretion of insulin more completely than other insulins. When this insulin is supplemented by a low starch intake, no postprandial rise of blood sugar need occur and cases treated in this way often exhibit a tendency toward the need of less insulin and sometimes the insulin may, after a time, be omitted entirely (Table V).

Since the protamine zinc insulin liberates insulin at a constant rate for more than 24 hours it would be expected that with marked restriction of starches in

TABLE VI

BLOOD SUGAR MG. %

Date	Insulin Units	Fasting	± 4 PM (After B & L)	Remarks
3/16	80 PZ	47	219	(While outside had large amounts sugar urine on same diet, doubtful whether adhered to, with 80 PZ, and 30 G). Control in hospital good with 80 PZ, though a low fasting B.S. was followed by a high B.S. at 4 P.M.—probably a rebound reaction from the hypoglycemia resulting in overproduction of sugar by the liver.
3/20	60 PZ	62	119	Perfect control production glucose and assimilation with less insulin.
3/23	50 G	86	129	Control perfect with still less insulin, some heavy sweating.
3/27	46 G	250	330	For two days preceding urine sugar-free with G 46; on this day laboring with the idea of going home, became very nervous and showed marked glycosuria. The over-response to stress manifested itself in the marked rise of blood sugar.

G. A., Male, aged 44, Diabetes 14 years.
3/16: Hyperglycemia, resulting from overdose of insulin.
3/27: Marked hyperglycemia due to nerve strain.
The impossibility of good control of the diabetes in this case is obvious. Evidently overproduction of glucose by the liver is readily brought about.

the diet the diabetes could be controlled by insulin injections every other day or even at longer intervals. An outline of such a case is given in Table II. When the diet was checked so that there was no postprandial rise of blood sugar the diabetes was fully controlled, but when this patient became careless about the starches eaten, glycosuria would appear. With no postprandial elevation of blood sugar the administration of protamine zinc insulin may be regulated with perfect safety according to the fasting blood sugar. Under these circumstances

the diabetes is completely controlled and all danger of hypoglycemic reactions are set aside.

The use of protamine zinc insulin resulted in a much more favorable response of tuberculosis in diabetes than was brought about by unmodified insulin (Mosenthal and Mark 1941)[13]. Wilder (1937)[14] showed that in cases of severe diabetes, intermittent periods of protein destruction and loss of nitrogen occur when unmodified insulin is injected at intervals, whereas tissue loss ceases when protamine zinc insulin is employed. This finding was offered as an explanation of the better effects of protamine zinc insulin. Whether resort to globin insulin with zinc or NPH will accomplish as much as protamine zinc, either in the cure of tuberculosis or the prevention of protein destruction, has not been tried out,

TABLE VII

HYPERTHYROIDISM, COMPLICATING DIABETES, CALLS FOR GREAT INCREASE IN INSULIN. THYROIDECTOMY RELIEVES THE INSULIN RESISTANCE.

Date	Blood Sugar* Mg. %	Urine		Regular Insulin Units	Remarks
		Glucose %	Acetone		
6/30/32	227	0	0	0	
10/6	227	0	0	0	
4/14/33	238	1.1	0	0	Mild hyperthyroid
9/9	235	2.0		30-30-35-20	Marked hyperthyroid
10/4	240	0.5	0	50-50-50-20-20-25	
10/5					Thyroidectomy
10/10	230	1.5		30-30-30-25	
11/8	240	0	0	16-8-16	

C. J., female, age 47. Mild diabetes until hyperthyroidism developed. The exacerbation of the diabetes could only be controlled by thyroidectomy.
*Fasting

but these facts are worth considering when resort is had to other insulins than protamine zinc.

A starch free diet results in build-up of protein and nitrogen retention when a large amount of protein food is eaten but an isocaloric replacement of proteins by fat or alcohol will not accomplish this (Mosenthal and Harrop 1918)[15]. Consequently on the low starch diets that are being advocated in this presentation it is urged that the protein intake should be very high.

This method of treating diabetes, while it is the ideal way to manage the disease, will fail when high starch diets are insisted on. This is unavoidable in

children and in many adults who apparently live to eat. Then recourse must be had to the insulins that act more markedly in the daytime during the period of heavy food ingestion and taper off at night. Regular insulin, globin insulin with zinc and NPH insulin, all have a place in fulfilling the needs of diabetics with slight or no restriction of starchy foods. If under these circumstances meals are delayed or the amount of carbohydrates eaten is not kept at a constant level there is the serious risk of hypoglycemic reactions.

Other factors requiring special attention for the checking of excessive glycosuria and the prevention of hypoglycemic reactions are the indulgence in hard exercise at irregular intervals, the effect of emotional strain or stress which may occur at rare intervals or almost continuously (Table VI), menstruation, pregnancy, infections, acidosis and coma, or other conditions resulting in increased insulin resistance, such as hyperthyroidism (Table VII).

Great conservatism must be practiced in correcting glycosuria by increasing or adjusting the dosage of insulin, since sugar in the urine may follow diet irregularities or the ingestion of large amounts of carbohydrate for the correction of hypoglycemia, which are only temporary effects. The immediate increase of insulin under these circumstances leads to a vicious circle of hypoglycemia, compensatory starch or sugar intake and an endless repetition of these happenings.

Summary and Conclusions

A 1 to 2 hour postprandial rise in blood sugar occurs in diabetics but not in normal persons. In diabetics a very low carbohydrate diet (or extra insulin) is required for the control of hyperglycemia after meals. The postprandial blood sugar is evidently a better criterion for the diagnosis and the management of diabetes than the fasting blood sugar.

A high level of blood sugar without glycosuria has no detrimental influence upon diabetes. Marked glycosuria, polyuria, dessication, lack of deposit of liver glycogen and protein destruction will have harmful effects upon the diabetic and it is in these changes that the cause for retinitis, nephritis, arteriosclerosis and coronary thrombosis, the frequent complications of diabetes, must be sought.

There is a difference in effect between the insulin secreted by the pancreas, endogenous insulin, and injected, exogenous insulin. Insulin secreted by the pancreas passes to the liver where a large part is retained for action upon the glucose carried by the portal vein from the intestinal canal to the liver. Insulin is in large part bound and retained in reserve by the tissue which it first contacts. Hence, endogenous insulin exerts its main influence through the liver while exogenous insulin affects principally the extrahepatic tissues.

A great leeway exists in the amount of insulin the body can take care of without changing the blood sugar from a normal level. The amount of insulin

usually secreted by the pancreas, the basic insulin, is probably greater than the body needs; some of this is stored in the liver for the full control of meals to come and some of it is taken up by the peripheral tissues to enable them to utilize glucose. As a rule, in normals, no extra insulin from the pancreas is required. The ingestion of large amounts of sugar by normals, however, or the eating of sugar-free but starch containing meals by diabetics, will result in a rise of blood sugar. In normals the pancreas responds, in fact over-responds, by secreting extra insulin; in diabetics there is a failure to respond.

It becomes clear that a starch-free diet or one with appropriate restrictions of carbohydrates will not result in a postprandial rise of blood sugar. In many diabetics this can be accomplished without the aid of insulin. When the basic insulin secretion is curtailed to the extent that the fasting blood sugar becomes elevated the use of insulin becomes obligatory. Protamine zinc insulin is the form of insulin which replaces the lacking basic insulin to the best advantage. When this insulin is resorted to and sufficient restriction of carbohydrate intake is maintained to prevent a postprandial elevation of blood sugar, then the diabetes may be regarded as completely controlled. There will be no danger of hypoglycemic reactions, the greatest chance for remission of the diabetes will exist, and all the possible measures for the prevention of complications will have been achieved.

There are many conditions which make it impossible to use this ideal plan. The unwillingness or inability of the patient to follow these dietary restrictions; hard physical exertion, especially at irregular intervals; menstruation; pregnancy; constantly recurring emotional disturbances; hyperthyroidism have been mentioned as among those conditions that call for the replacement not only of basic insulin but extra insulin as well. Extra insulin has to be supplied by insulins which act for less than 24 hours. Unmodified insulin, globin insulin with zinc or NPH insulin fulfill this requirement.

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THE DIFFERENTIAL DIAGNOSIS OF UPPER ABDOMINAL PAIN*†

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Although greatly flattered by your kind invitation to participate in this program, I must confess I had mixed feelings when I heard my specific assignment, the differential diagnosis of upper abdominal pain. I would not have had the temerity to select a subject so broad in scope, so variegated in etiology and significance, and often so baffling in interpretation. Nor was I so presumptuous to believe that I would have anything to say which you had not heard before. Nevertheless I thought it would be easy to catalogue the host of diseases capable of producing upper abdominal distress in some new arrangement and embellish this with some diagrams indicating the nerve pathways by which painful stimuli are conducted. It soon became apparent, however, that almost every conceivable tabulation has been tried and practically all of them begin with the false presumption that the diagnosis is known in advance. The pathways for the conduction of painful stimuli have been plotted with some degree of certainty but the application of such information at the bedside is attended with considerable difficulty. There are few areas in the human body which rival the upper abdomen in the frequency with which pain is felt and probably none with a greater number of local and remote sources for it.

After considerable deliberation these and many other approaches to the subject were rejected. There remained the personal method of approaching a diagnostic problem in which upper abdominal pain constituted a major complaint. This carries no implication that the ideas about to be suggested have any originality or superiority over other approaches; rather it is a restatement of the methods all of us employ more or less unconsciously. The fact of the matter is that the rules followed have become so universally known and so commonplace that they are threatened with oblivion in the midst of discussions of the laboratory approach to gastrointestinal problems.

One begins with the premise that Nature commonly employs an abnormality of sensation as the first indication of disease. Among these abnormal sensations, pain is outstanding not only because of its frequently early appearance but the readiness with which it is misinterpreted by the patient when as often few other symptoms exist. Generally speaking, pain unless severe, is not as prone to force a patient to seek medical assistance as many other symptoms, for example, bleeding. Moreover intensity of pain is often confused, by patient and physician, with the gravity of the situation. In this connection one may recall the agonizing

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pain associated with spasm of some portion of the gastrointestinal tract and the complete silence with which a gastric carcinoma may evolve to inoperability with little or no pain. At all events intensity of pain is no index of the seriousness of the situation.

Allusion should be made to two other points in these preliminary remarks which I trust will not prove too elementary. Since pain is a purely subjective phenomenon we must rely upon the patient's statements about it. There is, on the other hand, great complacency about accepting the patient's statement that real pain is present. Often a feeling of fullness, heartburn, and a host of other sensations are accepted as pain when they actually do not belong in this category. The other matter emerges from a common source of confusion, namely, the patient states that he has pain in the stomach when he means abdomen. Generally speaking when the patient talks about pain in his stomach reference is intended to distress associated with eating and not with an anatomical area; this distress may be located anywhere between the sternum and pubis. Two examples will suffice. A patient has pain immediately after eating, lasting for one or two hours. Since the pain is located in the epigastrium a gastric x-ray series is ordered and proves negative. Actually a carcinoma of the transverse colon may be attached to the posterior wall of the stomach so that tension is exerted during gastric peristalsis. We have been misled by the location of the pain and the association with eating. In another instance the patient has a carcinoma of the cecum. Immediately after eating pain is felt because of cecal distention as the result of mass peristalsis. Actually this pain is not felt in the upper abdomen but the association with eating is so definite that the patient as well as ourselves believes the distress is gastric in origin. Considerable progress has been made, I believe, when we are clear that a patient actually has pain and that it is located in the upper abdomen.

The next obvious question deals with the location of the pain. The fact that pain is noted in the midline is not particularly helpful since this happens in peptic ulcer, cholecystitis, gastroenteritis and a host of other disorders. Of greater interest is the location of the distress at a particular level in the midline.

In many diseases of the lower esophagus and of the cardia, there is accurate location of the pain in respect to the level of the lesion. Sooner or later most individuals with obstructing carcinoma of the lower end of the esophagus can point rather accurately to the level of the lesion. To be sure, mistakes occur and the distress may be indicated much higher than the site of the actual obstruction.

Since no further reference will be made to the esophagus and pain, one or two additional remarks may be of interest. As everyone knows the function of the esophagus is the transit of food and fluids. Consequently interference with transit often antedates pain, at least in the functional disorders of the esophagus. In cardiospasm, the dysphagia tends to be intermittent for a long time; sooner

or later it is associated with burning as well as a sticking sensation. The burning is of interest since it is associated with local increase of muscle tension and is independent of gastric acidity. This point has diagnostic as well as therapeutic import.

The epiphrenic syndrome of v. Bergmann should be mentioned because many now associate hiatus hernia and angina pectoris. It is common practice to subject patients with subxiphoid pain to roentgen examination in the Trendelenburg position. Not uncommonly a hiatus hernia is discovered and this discovery is employed to interpret an anginal pain. It is my increasing conviction that a relationship is actually rare although the association of coronary artery disease and hiatus hernia in a given patient is not at all unusual. While experimentally it has been demonstrated that distention of the esophagus in animals may alter myocardial perfusion, the clinical applicaion of this observation is, in my opinion, dubious. I suggest that most patients with hiatus hernia and with evidence of altered coronary perfusion of the myocardium should be regarded as having two coincidental but unrelated maladies, both of which require their individual therapy.

Another observation of some importance deals with carcinoma of the lowermost esophagus. There is, I believe, a good clinical rule: this states that carcinoma of the upper gastrointestinal tract ordinarily is not associated with spasm except when the lesion is at an orifice. This means that carcinoma at the cardia advancing upward in the lower esophagus may be associated with spasm; the pain and other symptoms sometimes may be relieved by antispasmodics. Unless this event is appreciated valuable time may be lost. Esophageal "peptic" ulcer usually provokes very high subxiphoid pain radiating to the back; pain usually occurs immediately after swallowing, and perhaps the only interesting feature is the immediate appearance of this distress after eating.

Returning now to other midline pains, one immediately thinks of the location of the pain in gastric and duodenal ulcer. These are seated lower than the pains just mentioned but still above the umbilicus. In an occasional patient the distress may be a little to the left or right respectively but the value of left- or right-sidedness often is overemphasized. Of greater importance here is the discovery of local tendeness somewhat to the left or right.

Pain in small intestinal lesions is poorly located but may be reported as periumbilical. Upper abdominal midline pain is not common in lesions of the colon except in an occasional patient with a lesion of the transverse portion. The high midline pain of acute appendicitis is of interest because subsequently it moves to its classical area. The same holds for the epigastric pain encountered in acute cholecystitis.

Before leaving the subject of midline pain, attention should be directed to another point. We are interested not only in discovering where the pain is felt but the gesture employed by the patient in pointing it out. The roving hand

which seeks the shifting pain and searches the entire abdomen in its quest points strongly in the direction of a functional lesion. The patient with an uncomplicated gastric or duodenal ulcer usually requires no more than the tip of one or two fingers to discover where it hurts. There is also little indecision in locating the pain at the site of ulceration after an anastomosis has been created for the relief of ulcer; usually the patient points just above and a little to the left of the umbilicus. If time permits we shall return to the subject of location in the right or left upper abdomen; at this moment we are concerned with adding to the analysis of a sensation and have stressed that the sensation actually is pain that it is felt in the upper abdomen and we have attempted to locate it more precisely by observation of the gestures.

Our next step is to form some judgment about the severity of the pain and every clinician rapidly evaluates this feature and his decision though based upon superficial evidence usually is reliable in proportion to his experience. If the patient is unknown to us and describing an earlier episode, one utilizes comparisons to judge the severity of the distress: was morphine or a hypodermic required for relief? Was the pain as bad as childbirth? Were the usual activities of the day impossible on the next day and the like?

The present speaker long ago gave up the Libman method for evaluating sensitivity to pain in individual patients. This test, as many will recall, depended upon the response to pressure over the styloid process when exerted by the thumb. As far as I am concerned the threshold to pain is about the same in all individuals; their responses and reactions to it as well as their descriptions show infinite variations.

There are many disorders associated with excruciating upper abdominal pain. Naturally one thinks first of a ruptured viscus, perhaps a ruptured peptic ulcer. In this instance the abrupt onset of severe pain, often radiating to the back plus shock, prostration and the early development of a boardlike abdomen usually make recognition easy; the syndrome of subacute perforation is much less dramatic and likewise readily recognized. The situation is similar in the pain associated with acute hemorrhagic pancreatitis although in this instance vomiting often dominates the clinical syndrome. Moreover, the back pain of pancreatitis often is aggravated by the recumbent position so that the patient prefers to sit or at least flex the body forward. Since we intend to use the pain of gallstone colic to illustrate some other features of pain, it will be merely mentioned at this point. The point to which attention is now directed is that the three syndromes mentioned, ruptured viscus, pancreatitis, and gallbladder disease may have pain referred to the precordium. Stated in another way, sometimes great difficulty is encountered in the differential diagnosis of these situations and coronary occlusion. Sometimes differential diagnosis may be impossible for, coronary occlusion may accompany rupture of a peptic ulcer. It is, however, more common for myocardial infarction to mimic ruptured peptic ulcer than for the reverse to occur. While the differential diagnosis may be difficult or impossible

in a particular instance, frequently there is overemphasis of the problem. When I had occasion to call attention to painless coronary occlusion with myocardial infarction nearly 25 years ago I was struck by the fact that coronary occlusion, presenting upper abdominal symptoms, often lacks the agonizing pain we tend to associate with the lesion. As a matter of fact most of these patients have what they call acute indigestion, insert a finger in their throat to produce vomiting, go to a drug store for an alkali and seek relief only after some hours elapse when the symptoms fail to disappear.

Often indistinguishable from myocardial infarction with upper abdominal symptoms is dissecting aneurysm in the profound weakness, and collapse disappearance of the pulse from one extremity or another should make the diagnosis apparent in most instances.

There is one lesion encountered infrequently but with a classical syndrome almost invariably overlooked until it is too late. Reference is intended to the individual who has just dined too well after excessive ingestion of alcohol. With the occurrence of a single episode of vomiting there appears agonizing pain which is followed by collapse and shock. Coronary occlusion may be suspected but is not present. After the lapse of a few hours, however, subcutaneous emphyzema is noted in the cervical region and the next morning an increasing left pleural effusion is discovered. On paracentesis the fluid reveals fragments of the food eaten and perhaps has the odor of the alcohol taken. So-called spontaneous rupture of the esophagus has occurred, a syndrome noted with increasing frequency in psychiatric individuals.

Having obtained a notion about the location and intensity of the distress we may also derive diagnostic information from the words employed to describe it. I observed many patients with "gnawing pain" before I made any effort to find out what was ordinarily meant by this description. With many individuals it is intended to describe pain which does not fluctuate in intensity while present. Thus the word may be used to describe the pain of peptic ulcer whereas the expressions often employed to describe the pain of acute gastritis imply a peristaltic character.

The importance of words in description of pain is illustrated by the phrase "gallstone colic". In point of fact the pain with cholelithiasis practically is never colicky. Colic means rhythmic intermittent griping pain but freedom from distress between the individual spasms. A careful review of case histories suggests that during the passage of a gallstone, the attack begins with a dull ache which progressively increases to become almost intolerable. It frequently repays the diagnostician to listen to the description of the pain as well as to watch the gestures associated with the description. Local burning as encountered in ordinary heartburn is annoying, uncomfortable but practically never agonizing. Moreover it is rarely associated with organic disease. On the contrary diffuse abdom-

inal burning intractable and widely diffused over the abdomen is a common phenomenon in emotional disorders and in psychiatric patients.

It would be impertinent of me to recite the various classical types of radiation of pain to this audience. On the other hand it may be permissible to mention to gastroenterologists that it is not uncommon to encounter right upper quadrant pain when the basic malady is outside of the abdomen.

Right hypochondrial pain associated with vomiting is a very common event in acute episodes of congestive heart failure and generally is explained by acute engorgement of the liver and stretching of Glisson's capsule. Often this is overlooked particularly when the cardiac failure is not recognized, for example in a prolonged paroxysmal tachycardia. This reference to congestive heart failure recalls another cause of right hypochondrial pain frequently mistaken when associated with local muscle guarding and perhaps evidence of ileus. Reference is intended to diaphragmatic pleurisy following pulmonary infarction in a patient with congestive heart failure. With these illustrations, which need not be multiplied, we have indicated the necessity for eliminating thoracic diseases such as basal pneumonias, pericarditis and the like in the evaluation of upper abdominal pain.

While we are deeply interested in the duration of the pain and, when pain has been experienced over a long period, changes in its character, ordinarily more information is derived from the factors associated with the appearance of the pain and its relief. The classical cycle of food and pain in uncomplicated ulcer need not detain us, but passing allusion may be made to the change of the relationship when complications occur. Thus, we may form some general rules like the following: pain in the epigastrium, recurring daily with definite reference to the intake of food is probably gastric in origin; pain appearing out of a clear sky without relation to eating or exercise is suggestive of a tabetic crisis or cholelithiasis and so on. Our inquiries may be directed at other elements of rhythmicity: the episode of angina pectoris in the first few hours after retiring; the night pain of duodenal ulcer developing around midnight; the attack of gallstone colic in the early morning hours and so forth. Other elements of aggravation or relief should excite our interest. Upper abdominal pain awakening a patient from sound sleep is not uncommon in various forms of spondylitis. Pain produced by sneezing, coughing, straining at stool is noted in radiculitis and some vertebral and spinal lesions. Pain not evoked by deep palpation but produced by jolting may be seen in connection with stones in the gallbladder as well as in the kidney although relatively few renal disorders are associated with upper abdominal pain.

While our unconscious analysis of the pain is proceeding we have also been forming other judgments. In our attempt to locate the pain accurately we may perform a pinch test since undue pain on pinching may be associated with lesions in the abdominal wall. for example, in fibromyositis. More definitely we should

note guarding of the area by the muscles and should search for local soreness. Local soreness often persists in organic disease long after the spontaneous pain has stopped; this is particularly true of peptic ulcer. This situation stands, as a rule, in strong contrast to that of gastric carcinoma. In the latter guarding usually is absent so that the abdomen of a patient with gastric cancer usually is extremely accessible to examination. If epigastric guarding is noted in this disease, usually it is bilateral and its appearance is postponed until evidence of peritoneal invasion is apparent.

The use of the word peritoneum in the last sentence reminds me that I have failed to mention this important membrane, the blood vessels of the abdomen and many other structures. I have failed to indicate the different incidence of local and referred pain in visceral disease versus functional disorder and a host of other topics.

In summary, an attempt has been made to analyze some ordinary features of a single symptom, namely pain in the upper abdomen. Reference has been made to ten characteristics which I believe every one unconsciously considers in connection with it. If one or more of them are neglected the opportunity for diagnostic error increases.

Had time permitted, the particular types of pain encountered in malfunction of each provocative organ could have been analyzed in a similar way. If we superimpose upon this, the additional modifications observed when the basic pathology, inflammation for example, is considered we have gone far in establishing a reasonable basis for an intelligent physical examination and informative laboratory investigation. It seems to the present speaker that a similar analysis of other outstanding symptoms in gastroenterology greatly contributes to a proper diagnostic approach.

RECTAL BLEEDING*

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Blood per anum can originate from any part of the gastrointestinal tract (lips to anus). Bleeding is one of the most frequent symptoms associated with diseases of the anus, rectum and sigmoid and its presence should call for a most thorough proctoscopic examination. This is a big subject and of great concern to the general practitioner. In the majority of cases the cause of blood loss per rectum can be detected by proctoscopic or sigmoidoscopic examination. Radiography should be utilized to detect causes above this area.

Until a few years ago, patients rarely consulted the doctor for rectal bleeding alone, unless it was accompanied by pain, swelling, etc. In the mind of the public it was usually associated with "piles". Since the public has become cancer conscious, more patients are coming to doctors for diagnosis and treatment of rectal bleeding. A hundred causes of rectal bleeding have been reported in the literature and it is not my purpose to enumerate them all. The presence of blood in the stools in any form should suggest immediately to the physician's mind the possibility of carcinoma until the cause can be proved otherwise.

Blood may be present in the stools in 2 forms.

a. Unaltered blood where the morphological characteristics of the red blood cell remains unchanged. This may be of sufficient quantity that it can be seen macroscopically, or be so slight that it can only be identified microscopically.

b. Occult blood is present in the feces only when blood has been in the intestinal tract a sufficient length of time to permit its decomposition. The passage of this altered blood is known as *melena*. As little as 50 c.c. of blood in the stomach may cause tarry stools. If amounts are less the blood can be detected only by chemical tests. Before making a diagnosis of "occult blood" one must remember that drugs such as iron, bismuth or charcoal may cause "dark stools". The diagnosis of occult blood should always be made on a meat free diet, otherwise we may get a false positive. Bright red color in the stools may be caused by beets or other highly colored foods.

In discussing rectal bleeding we must first determine, if possible, the site of the bleeding and secondly the underlying pathological condition. The treatment is dependent on the cause.

I like to separate this subject into infants, children and adults, and further subdivide these into general and local.

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In infants and children the general causes are melena neonatorum, Henoch's purpura, extensive burns (Curling's ulcer), septic infection of the umbilicus, Meckel's diverticulum, marasmus, malnutrition, epidemic diarrhea and bacillary dysentery. A percentage as high as 21.5 in a series of 293 cases of melena has been reported. Forty-six cases occurred in the first decade of life.

The most common local causes of rectal bleeding in infants and children are fissure and polyps. Hemorrhoids very rarely occur in children. Prolapse of the rectum, especially if it has protruded for any length of time may result in rectal bleeding. Trauma as a result of impalement injuries, enema tips, thermometers or foreign bodies may cause bleeding. Congenital anomalies which have been corrected, leaving considerable scar tissue often bleed. Thread worms (oxyuris vermicularis) often cause both blood and mucus in stools.

In adults the general causes are leukemias, anemias, hemophilias, purpura hemorrhagica, splenomegaly, cirrhosis of the liver, chronic nephritis with uremia, cardiac disease, Weil's malignant jaundice, mesenteric thrombosis, esophageal varices and pancreatic embolism; one case of pancreatic Ca with metastasis to the colon; typhoid fever, dengue, pellagra, yellow fever, cholera, smallpox, scurvy; poisoning by heavy metals, arsenic, Hg., vicarious menstruation, malaria and tuberculosis; hiatus hernia with a pinching of the gastric mucosa (ulcer). While the above conditions are problems for the internist, the proctologist must keep them in mind.

Local bleeding of traumatic origin may be due to foreign bodies, chicken or fish bones, enema tips, large foreign bodies of bizarre kinds, vegetables, bulbs, etc.; fecal impactions, i.e. impaction adherent to rectal wall with subsequent ulceration; surgical injuries, following prostatectomy, pelvic repairs; penetration injuries, i.e. impalement wounds or gun shot wounds or pneumatic injuries; fractured pelvis, producing puncture of the rectum by spicules of bone may produce severe hemorrhage. In dealing with trauma of the rectum one must differentiate between wounds that have entered the peritoneal cavity and those that have not.

Postoperative hemorrhage following hemorrhoidectomies or any other rectal operation may be immediate and is due to faulty operative technic, or it may be secondary, usually 7th or 8th day due to slipping or sloughing of ligatures and exposing the vessel in the granulating wound.

Perianal bleeding can be attributed to condylomata accuminata or lata, anal chancre, tuberculosis of the anus, anal chancroid, actinomycosis and blastomycosis (granulomatous). Epithelioma, melanoma, pruritus as a result of trauma, abscess and fistula.

In fissure-in-ano the bleeding is usually slight, occurring only during the act of defecation. The quantity of blood is small and sometimes only noticed

on toilet paper. Feces streaked with blood in a line either posteriorly or anteriorly; indicating even to the patient the site of the lesion.

Infected crypts and inflamed papillae will cause slight amounts of blood.

Mucosal prolapse and true procidentia will also produce bleeding. Bleeding in the latter is constant, requiring the wearing of a pad. Proctoscopy in these cases reveals a thickened and redundant mucous membrane with superficial inflammation and ulceration.

The most common source of unaltered blood are hemorrhoids and the bleeding is a result of erosion or ulceration of the vessel wall. The bleeding at first only occurs at defecation; either streaking the stool or it may spurt out with considerable force, discoloring the bowl. The quantity of blood lost varies according to the size of the damaged blood vessel. Where there is no protrusion this bleeding stops automatically. Where the hemorrhoids protrude, however, bleeding may occur apart from defecation and underwear is usually soiled with blood. The mere presence of hemorrhoids which are obviously bleeding does not relieve one of the responsibility for a thorough examination. Such hemorrhoids may be caused by an infiltrating lesion above, which obstructs venous return and thereby increases the venous pressure of the hemorrhoidal system. I have seen several cases of severe hemorrhage (Hgb. 6 to 7 and R.B.C. of 2,000,000) resulting from ulcerated hemorrhoids. It is well to rule out hemorrhoids as the cause of secondary anemia.

External thrombotic hemorrhoids that have ruptured will also cause rectal bleeding.

Next to hemorrhoids, polyps are the most frequent causes of bleeding per rectum. Benign adenomatous polyps produce slight bleeding where the surface is ulcerated and especially if the polyp has a pedicle and protrudes within the sphincter mechanism; obscure until you find the polyp. In multiple polyposis the blood is mixed with mucus and pus.

Villous adenoma, which is usually sessile and situated on the posterior or lateral wall of the rectum may at times produce severe hemorrhage with mucus. This is considered a low grade malignancy.

The bleeding and the character of the stools in cases of carcinoma of the rectum depend on the stage of the development of the growth. In early stages, traces of blood are passed intermittently. When ulceration takes place there is usually a continuous serosanguinous discharge. Neoplastic lesions of the anus, rectum and rectosigmoid usually produce bright red blood, while lesions higher up produce the so-called tarry stools. Lesions above the sigmoid at first may only show occult blood and when this is found one should be careful of its proper assessment. Progress of the blood pattern from 4 to 3 to 2 million in 6 to 8 weeks is important. Carcinoma of the right side is a frequent cause of anemia. Blood is usually dark in color or discovered by chemical determination.

Proctitis either specific or nonspecific may produce bleeding. The quantity of blood as a rule is not large, since the bleeding points are usually superficial erosions of the rectal mucosa. If perforation occurs, the bleeding is profuse.

Any simple enterocolitis that has lasted for considerable length of time may produce blood in stools. Chronic hypertrophic proctitis usually does not cause bleeding, but the atrophic type does.

The dysenteries; Amebic, bacillary and chronic ulcerative types all produce blood. Lymphopathiavenerium, Tbc and schistosomiasis will cause blood in stools. Factitial or radiation proctitis should be considered when patients are undergoing x-ray or radiation therapy. Endometriosis as a rule does not produce rectal bleeding unless ulceration has occurred at the rectovaginal septum.

Diverticulitis: Bleeding is slight and is usually associated with pain, mass, low grade fever. About 30 to 40 per cent of patients with diverticulitis will pass bright red blood.

Stricture of the rectum of whatever origin causes bleeding as a result of ulceration either above or below the stricture. Bleeding as a rule is slight.

Occult blood as a rule is due to lesions high up in the gastrointestinal tract. Esophagus, stomach (ulcer, Ca, varicosities). Also from teeth, gums, nasopharynx, lungs, etc. In certain cases lesions high up may cause bright red blood on account of increased peristalsis, or if the quantity of blood lost is great, the blood is only partially altered.

Conclusion

The importance of the role of the internist in making an early diagnosis in cancer of the gastrointestinal tract cannot be stressed too strongly.

For a positive determination of the cause of bleeding it is essential for the internist and proctologist to make a thorough search. This can only be accomplished by a careful history and a complete proctosigmoidoscopic examination; augmented by stool studies, bacteriological studies and x-ray examination.

BLEEDING FROM THE GASTROINTESTINAL TRACT*

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When bleeding occurs from the gastrointestinal tract, as hematemesis or melena, or when occult blood is present in the stools, both patient and physician should become concerned and immediate steps should be undertaken to ascertain the cause.

As you will see at a glance, the causes of bleeding from the gastrointestinal tract are many, and frequently only after a very careful search by history, physical examination, x-ray, gastroscopic and sigmoidoscopic examination, can a satisfactory diagnosis be arrived at. A full discussion of all the causes enumerated is not possible in the allotted time. Some of these causes will merely be alluded to; others only briefly discussed.

Bleeding from the gastrointestinal tract may be due to:

1. Thrombocytopenic purpura
2. Henoch's purpura
3. Leukemia
4. Osler-Goldstein hereditary telangiectasis of the stomach
5. Typhoid Fever
6. Weiss-Mallory syndrome
7. Esophageal varices
8. Diverticulum of the esophagus
9. Hiatus hernia
10. Mesenteric embolism or thrombosis
11. Intussusception
12. Ulcerative colitis
13. Acute superficial and chronic hypertrophic gastritis with superficial erosions
14. Polyps (stomach, duodenum, colon, rectum) diverticulosis
15. Carcinoma of the gastrointestinal tract [esophagus, stomach, duodenum, (rare), small intestine, colon, rectum]
16. Peptic ulcer (esophagus, stomach, duodenum, jejunum, Meckel's diverticulum)

This tabulation in no way reflects the frequency or the relative importance of these various conditions.

The finding of internal hemorrhoids as a source of the bleeding should not put the physician at ease as, not infrequently, other pathology may also be

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present. It is not at all unusual to find polyps or carcinoma masked by the presence of the bleeding hemorrhoids. Blood loss through the gastrointestinal tract may be a slow seepage producing varying grades of anemia, or the blood loss may be massive, producing varying degrees of shock as well as sudden severe anemia.

1. *Thrombocytopenic purpura:*—Here the purpuric areas on the skin and mucous membrane will give the clue to the probable cause of the gastrointestinal bleeding. Low platelet count, prolonged bleeding time, delayed clot retraction and the tourniquet test are confirmative evidence.

2. *Henoch's purpura:*—The cramp-like abdominal pain, a palpable spleen, skin lesions and melena will direct attention to the cause of blood in the stools.

3. *Leukemia:*—The leukemias should offer no great difficulty in diagnosis. The acute leukemias with swelling, ulcerations, and bleeding from the oral cavity and occasional bleeding from the various areas of the gastrointestinal tract can be readily recognized by blood examination and sternal puncture. The usual physical findings of fever, anemia, enlarged lymph nodes and spleen are present.

4. *Osler-Goldstein hereditary telangiectasis of the stomach:*—Bleeding may occur from the multiple dilatations of the capillaries and venules of the skin and mucous membranes of the oral cavity and the mucosa of the stomach. Bleeding may occur intermittently over a period of years. The diagnosis of hereditary telangiectasis of the stomach may be suspected when lesions of the mucous membranes of the mouth are present. The presence of these lesions in the stomach may be confirmed by gastroscopic examination as first described by Renshaw in 1939.

5. *Typhoid fever:*—Ulcerations of Peyer's Patches in the ileum produce bleeding of varying severity, often massive and repeated until shock and frequently death supervenes. During the epidemic of 1903-4-5, when I was a medical student and interne, the wards were filled with typhoid cases. Melena was exceedingly frequent, occurring in about 25 per cent of the hospitalized cases. It was one of the principal causes of death, especially when complicated by perforation. The diagnosis of typhoid fever in the second and third week when hemorrhages occur, is relatively easy. Today, typhoid fever is a rare disease and the prognosis is much better, due to the antibiotics and replacement therapy of blood loss by transfusions. I recall the case of a young man admitted to the ward about ten years ago, who presented all the clinical features of typhoid fevor, a characteristic fever curve, roseola, a palpable spleen and even a dicrotic pulse. After a few days, diarrhea with tarry stools occurred, making a diagnosis of typhoid fever practically a must, clinically. The Widal, however, remained negative, no typhoid organisms could be recovered from the stools or urine, and at autopsy, ulcerations in the ileum were found, practically confirming the diagnosis of typhoid fever. But no typhoid organisms could be cultured and the final pathological report was "Lesions due to allergy to the sulfanilamides which were taken prior to admission to the hospital, causing tissue sensitization with subsequent shock producing

irreversible necrotic and inflammatory changes which may occur anywhere in the body."

6. *Weiss-Mallory Syndrome:*—Weiss and Mallory described instances of massive hematemesis occurring after persistent retching and vomiting. At autopsy, fissure-like lesions at the juncture of the esophagus and cardiac opening of the stomach were found. These events followed alcoholic debauches. Under these circumstances one might think of this syndrome, but a clinical diagnosis would hardly be possible. (I have never seen an instance of this condition.) The reported instances were found at autopsy. It is conceivable that lesser grades of ulceration and less intense hemorrhages may end in recovery. Esophagoscopy, which can be performed with greater ease today, could reveal these lesions and by the use of tamponage, hemorrhage might be controlled and a fatal outcome averted.

7. *Esophageal varices:*—In gastrointestinal bleeding of unknown origin, do not fail to look for esophageal varices. With barium and water, equal parts, the x-ray of the esophagus will reveal translucent areas, especially in the lower third of the esophagus, appearing as beaded-like areas (Fig. 1). The diagnosis of esophageal varices may be made when the vomiting of blood, and tarry stools, with enlarged liver and a palpable spleen or ascites with enlarged veins on the abdomen and vascular spiders or angiomata on the skin, are present. It can be confirmed by x-ray and esophagoscopy. Tamponage, injection of the varices, and one of the shunt operations are available for the control of the bleeding.

8. *Diverticulum of the esophagus:*—This, when inflamed, may cause bleeding. X-ray will readily reveal the presence of the diverticulum.

9. *Hiatus hernia:*--Bleeding from superficial erosion or ulceration in a hiatus hernia is not unusual. X-ray examination may or may not disclose the presence of the ulceration (Fig. 2). The presence of blood in the stool, or a massive hemorrhage, or an unaccounted-for anemia should make one think of the presence of a hiatus hernia. It is now routine practice of the roentgenologists to look for the presence of a hiatus hernia; yet, when found, they, as well as many internists, believe that a hiatus hernia is symptomless. My own experience is quite different. I make the bold statement that I have yet to see one that is completely silent, over a long period of time. Symptoms may be present only intermittently, when the herniation is caught by spasm of the ring, producing sudden sharp pain at the lower end of the sternum, which may radiate precordially or into the back. The pain may last a few minutes and be relieved suddenly by belching. These symptoms may be mistaken for angina, biliary colic and ulcer. When esophagitis or a superficial erosion is present in the herniation, persistent burning pain, substernally, coexists for days or for several weeks, and is practically constant. X-ray examination may fail to reveal the cause, and a diagnosis of neurosis is the result. These symptoms may recur at intervals of weeks, months or even years, and when an unaccounted-for anemia with occult blood in the stool, or a massive

hemorrhage appear, a search will reveal the cause and a correct diagnosis is made. In the past two or three years, we have found hiatus hernia more frequently because it is looked for. The history and the symptoms presented have become so familiar that the correct diagnosis can be suspected.

10. Mesenteric embolism or thrombosis:—Bleeding from the bowel is one of the cardinal symptoms of a mesenteric embolism or thrombosis in association with severe and relentless intermittent cramp-like pains in the abdomen. The diagnosis can be made if the patient happens to be fibrillating at the time of the examination. If these symptoms are present and no bloody stool has yet been passed, a proctoscopic examination will reveal blood in the bowel. I reported four instances. The diagnosis was made when the patients were first seen and they

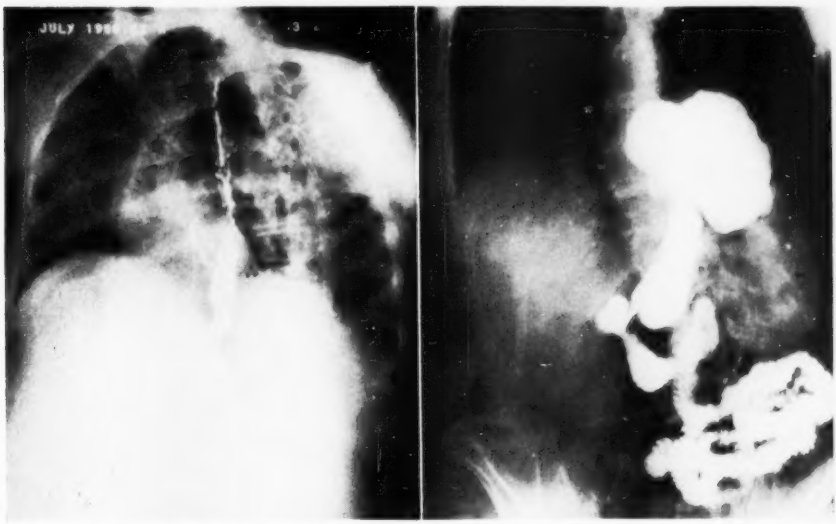

Fig. 1

Fig. 2

were all promptly operated upon. Resections of the gangrenous bowel were done. Unfortunately, none of the patients recovered, too long a time having elapsed before surgery was instituted. In addition, the circulatory embarrassment and the presence of varying degrees of shock made the prognosis unfavorable.

11. Intussusception:—In an infant with tenesmus, bloody mucus in the stool and persistent cramp-like pain, intussusception should be suspected. A scout plate of the abdomen and a small barium enema will confirm the diagnosis. The same symptoms are present in adults with carcinoma of the small, and especially, the large bowel, when partial obstruction is present and intussusception occurs.

12. Ulcerative colitis: Bleeding of varying intensity in ulcerative colitis occurs in every instance (Fig. 3). The amount of blood lost may be minimal or

massive. The bleeding may be persistent and is present in every evacuation. Twenty or thirty stools in twenty-four hours is not unusual in severe ulcerative colitis, and they are composed chiefly of blood and pus. The characteristically intensely inflamed, edematous, friable bowel which bleeds easily and is studded with erosions can be readily seen proctoscopically.

13. Acute superficial and chronic hypertrophic gastritis with superficial erosions:—Bleeding may occur from these lesions and may, at times, be quite severe. These superficial erosions cannot be detected by x-ray, but can be visualized gastroscopically. We have instances where subtotal gastrectomy was performed

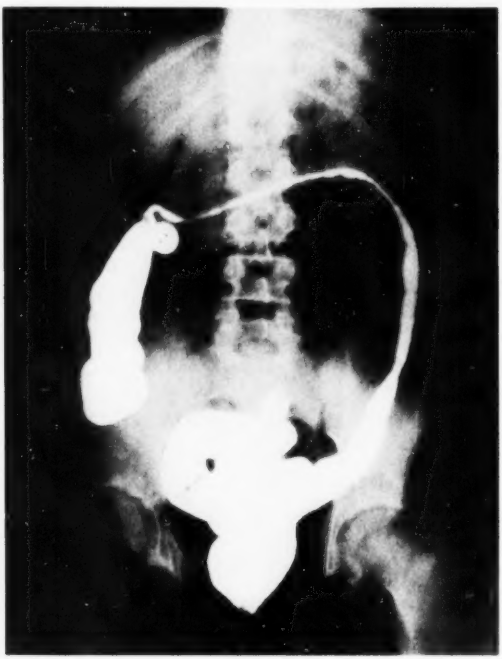

Fig. 3

for massive hemorrhage and the specimens revealed a gastritis. After careful search a minute superficial erosion overlying a vessel was discovered as the source of the bleeding.

14. Polyps:—Polyps of the gastrointestinal tract are frequent causes of bleeding from the gastrointestinal tract (Fig. 4). They are potential cancers and should be removed. We see patients who had rectal bleeding intermittently over a period of months and years. Some had a hemorrhoidectomy but their bleeding recurred. Thorough preparation for a satisfactory examination is imperative. When a polyp can be visualized through rectosigmoidoscopy, the diagnosis is simple. But one

must remember that there may be polyps higher up, beyond the reach of the scope (Fig. 5), and no examination should be considered adequate without a contrast air injection. The elusiveness of a single polyp in the colon is demonstrated by the following case:

A middle-aged man had a left inguinal hernia repaired. While still in the hospital, he complained to his surgeon that he was bleeding from the rectum. The surgeon found hemorrhoids which he removed. Before the patient left the hospital he told the surgeon that he had bled again. He was assured that he was all right. Soon after leaving the hospital, the bleeding recurred, forcing him to seek advice elsewhere. A satisfactory examination revealed the presence of a polyp in the sigmoid, seen by contrast air injection. The patient was referred to

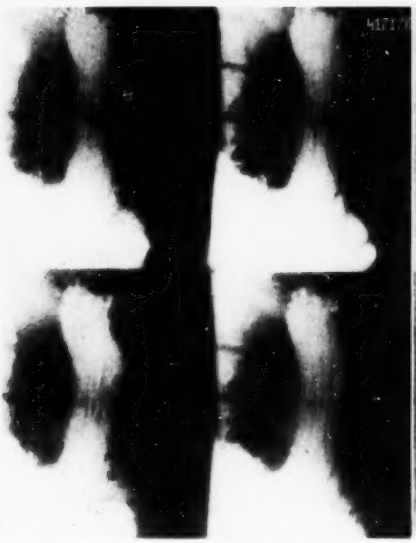

Fig. 4

Fig. 5

a surgeon who opened the bowel at the site of the polyp in the sigmoid. He could, however, neither see nor feel it. He closed the bowel, took out the appendix, and told the patient he could not find the polyp. This man returned, was indignant and demanded an explanation why such a mistake had been made. He submitted to a re-examination, and again the presence of the polyp was demonstrated. This diagnosis was confirmed at another clinic and the polyp was later successfully removed. His father died of a polypoid carcinoma of the sigmoid.

An eight year old boy with a large polyp was brought in by his mother who sought advice because of rectal bleeding which was present intermittently for more than a year. This boy was an extremely cooperative little patient and a sat-

isfactory examination could be made. After adequate preparation, a sigmoidoscopic examination revealed a small amount of bloody mucus beyond the end of the sigmoidoscope. The bleeding was apparently from higher up. Barium enema was negative. (Quite commonly a barium enema fails to reveal the presence of a polyp.) Contrasted with air, a large polyp came into view (Fig. 6). It was successfully removed.

Polyps may be single or multiple and they may be present anywhere, in the stomach, duodenum or colon (Fig. 7). When polyposis of the entire colon is present, a complete colectomy must be done. Bleeding is the most constant symptom of the presence of polyps.

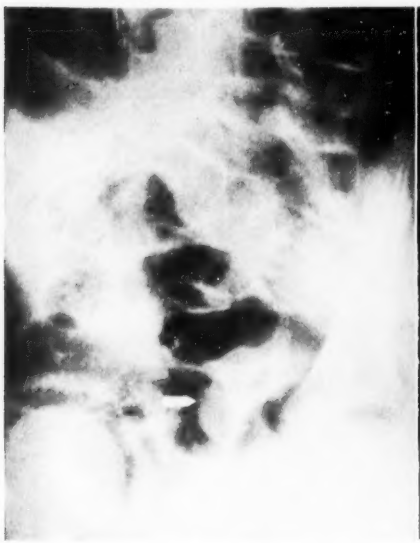

Fig. 6

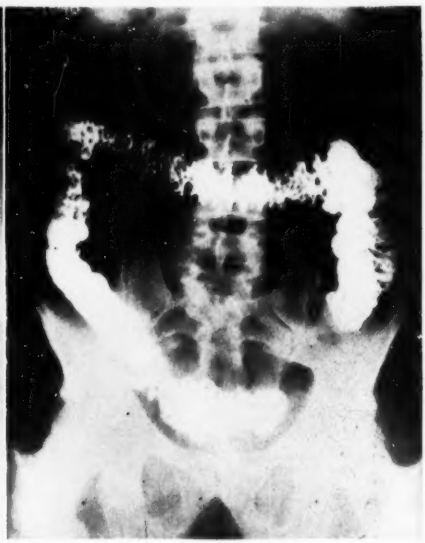

Fig. 7

15. Carcinoma of the Gastrointestinal tract:—When bleeding occurs from the gastrointestinal tract, the first thought is to rule out carcinoma. Bleeding from carcinoma in the gastrointestinal tract is usually slow, and not massive, except in ulcerating carcinoma of the stomach, where the bleeding may become exsanguinating. In older individuals, particularly, a massive hemorrhage from the stomach is likely to be due to peptic ulcer or an ulcerating carcinoma (Fig. 8). Carcinoma of the esophagus (Fig. 9), duodenum (which is rare), small intestine, and carcinoma of the colon, all bleed usually in minimal amounts, over a relatively long period, producing a hypochromic anemia. The bleeding is usually not massive as in peptic ulcer or ruptured esophageal varices. In the past two years we have encountered the only three cases of carcinoma of the jejunum—opposite the ligament of Treitz which we have seen (Fig. 10). All three were

successfully resected, and thus far, have remained well. The symptoms were cramp-like pains, bloating and on several occasions, blood in the stool.

16. Peptic ulcer:—The most frequent cause of bleeding from the gastrointestinal tract other than hemorrhoids is peptic ulcer (Fig. 11). The ulcer may be located in the esophagus, stomach, duodenum or Meckel's diverticulum (Fig. 12). Bleeding from ulcer may be minimal, moderate or massive and rapidly exsanguinating (Fig. 13). Under proper management, lesser grades of bleeding will become arrested in practically 100 per cent of cases. Continued or recurrent bleeding becomes more of a problem, and massive hemorrhage a serious threat to life.

Treatment of massive hemorrhage of peptic ulcer origin:—If confronted with a patient with a massive internal hemorrhage, the task of determining the source of the bleeding is, as we have seen, not simple. I will limit my discussion at

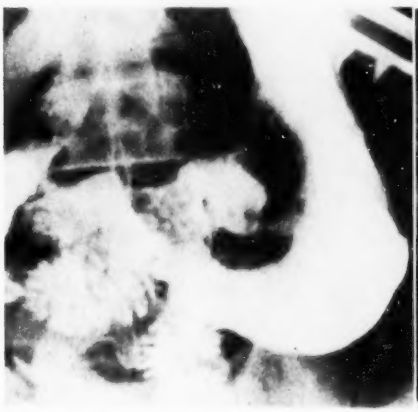

Fig. 8

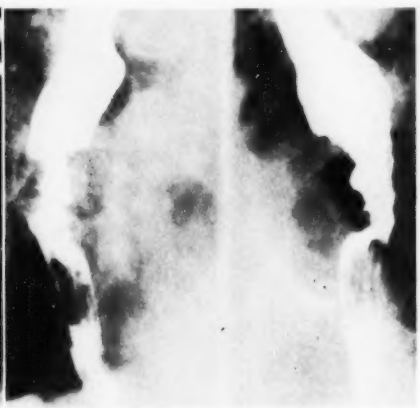

Fig. 9

present to those instances where the hemorrhage is from a peptic ulcer, the diagnosis of ulcer having been established prior to the occurrence of the hemorrhage. When characteristic symptoms of ulcer preceded for varying periods of time, the occurrence of the hemorrhage and a probable diagnosis of ulcer may be assumed. Since I wish to limit my discussion chiefly to the treatment of massive hemorrhage, I shall define what I mean by massive hemorrhage.

Massive hemorrhage is a large blood loss, occurring rapidly, becoming exsanguinating and attended by varying degrees of shock. The red blood count drops rapidly to two million or less, accompanied by a marked fall in blood pressure, accelerated pulse rate, profuse sweating, varying degrees of faintness, marked pallor and air hunger. All of us have encountered these instances and doubtless, we were impressed with the serious threat to the survival of the patient. This condition obviously excluded instances where only an occult seepage

is taking place, or a mild or very moderate blood loss has occurred. In these instances, there is no shock and there is no immediate threat to life.

Hemorrhage of varying intensity is said to occur in about twenty-five per cent of peptic ulcer. My own experience would put this figure much lower, excluding, of course, occult seepage. Hemorrhage from duodenal ulcer occurs about four times more frequently than in gastric ulcer, the tendency to hemorrhage is just about equal. Men are about twice as prone to hemorrhage as women. There is also a greater incidence of duodenal ulcer in men.

Hemorrhage as a first symptom of ulcer is rather frequent. (Occurs in about 16 per cent of cases, according to Ivy.) My own experience does not confirm this

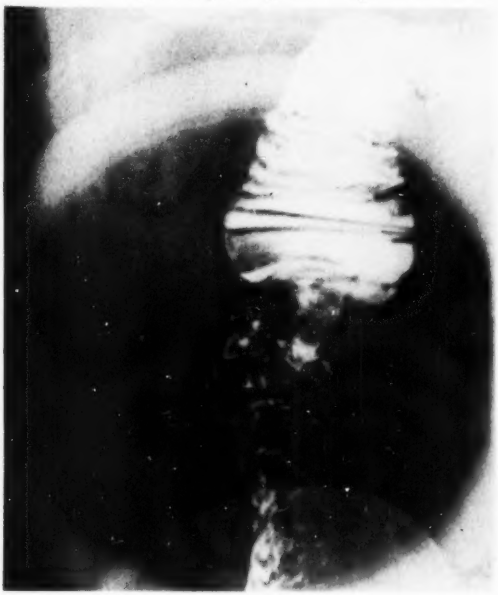

Fig. 10

high figure. Here, too, one must differentiate a mild seepage from frank hemorrhage.

Up to recently we were taught to treat hemorrhage from the digestive tract, due to ulcer, with rest, morphine, starvation and watchful waiting. This was the accepted therapy for many years. Later, transfusions and replacement therapy were added and about twenty years ago, Meulengracht introduced liberal and early, in fact, immediate feeding. The mortality under this conservative medical regime varied widely—since all grades and all types of hemorrhage were included. The mortality from massive hemorrhage is four to six times as great as stated in the overall statistics which includes all grades of bleeding, or not a

four to five per cent, but a 30 per cent mortality. Mild to moderately severe hemorrhage with a mortality of only four or eight per cent is recorded in a large series of cases. Obviously then, the approach to treatment must be quite different in these two classes of cases.

Age is also recognized as an important factor in the prognosis. All observers are in agreement on this point. Under forty-five, the mortality from hemorrhage is much lower, than above fifty years of age, and the mortality keeps on increasing with advancing years, the reason being that the vessels have lost their contractibility and clotting cannot occur readily. Pollard and Wallum reported a 38.7 per

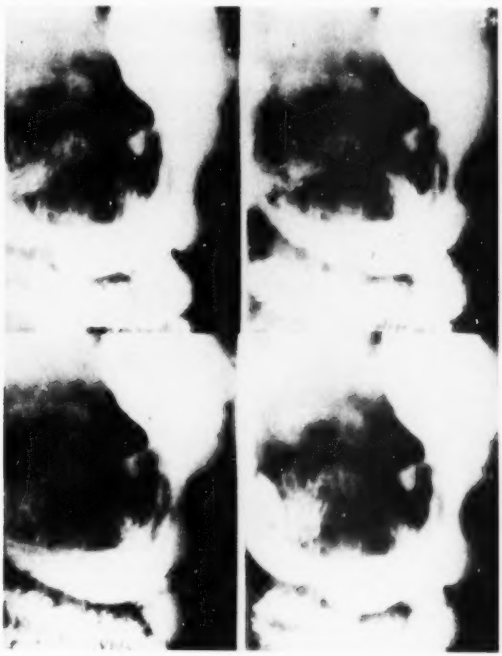

Fig. 11

cent mortality in a group of 31 cases of rapidly recurring hemorrhages, that is massive hemorrhages.

The reading of blood urea estimations on successive days has been advocated as an index of the gravity of a hemorrhage. Chinn and Harkins and Schiff have called attention to the relationship of the blood urea level to prognosis. In massive hemorrhage, one cannot wait to follow this guide. Prompt, radical measures must be instituted.

If a patient with massive hemorrhage is seen in the home, therapy can and should be instituted immediately–the replacement of the blood loss by plasma

is begun and the patient is dispatched to the hospital. In previous times, we debated whether it was safer to keep the patient at home and not disturb him for fear of aggravating the bleeding, or risk moving him to the hospital where the situation could be handled more satisfactorily. Today, I think most of us are convinced that the patient has a better chance in the hospital, where a team is alerted and waiting and the proper set-up is ready to start transfusions of whole blood immediately. An interne or preferably a resident who is familiar with the problems involved, and with previous experience, a special nurse, and an ample supply of whole blood, a blood bank being available, are ready and waiting. I have seen inexperienced internes fumble around trying to get into the collapsed vein—losing valuable minutes. An experienced resident or attending surgeon, by cutting down on the vein, starts the transfusion immediately. From then on, the

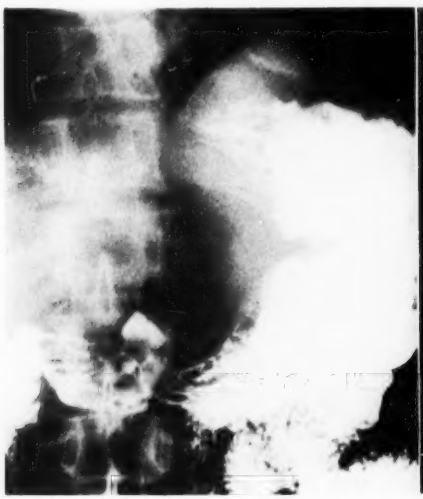

Fig. 12

Fig. 13

patient must not be left alone—the interne and special nurse are in constant attendance until shock is overcome and the patient is taken to surgery. These details seem trivial, but I have seen, on more than one occasion, the lack of these necessary services directly responsible for the death of the patient, who, otherwise, may have survived. When a patient bleeds to death right under one's eyes, because of fumbling and bungling attention at a critical time, one becomes impressed. Replacement of blood loss by transfusions of whole blood is kept up until the blood pressure rises, pulse rate and respiration improve and symptoms of shock are overcome. This may require 1,500-2,500 c.c. of blood and it may take several hours to turn the tide. Then, an experienced surgeon and his team, including the anesthetist, preferably perform a subtotal resection as a matter of choice. Obviously, a well-organized hospital set-up, including a blood bank and

an experienced surgical team are essential for the best results. If this is not available, then I would rather trust to watchful waiting, transfusions, etc.

There are surgeons as well as medical men who prefer to treat massive hemorrhage due to peptic ulcer conservatively with a reported mortality of ten per cent and as high as thirty per cent. Cases operated on late, after exsanguinating bleeding, and after failure of medical measures, result in a very high mortality, more than fifty per cent. These autopsied cases revealed severe circulatory damage due to long-standing anoxemia resulting in myocardial insufficiency, right heart failure and coronary thrombosis.

Had these same cases been operated early in the first hours of hemorrhage (and thus been spared these late complications), they could have been successfully resected with a very low mortality.

My own experience with the immediate surgical treatment of massive hemorrhage due to ulcer has convinced me of its merits and the better results are impressive when compared with expectant medical management or late surgery.

If a proper set-up and teamwork with an experienced surgeon are not available, it is better to wait and treat even a massive hemorrhage medically. If a patient with an ulcer has bled and recovered under medical management, there is no guarantee that he will do so the next time he bleeds, especially when hemorrhage recurs at a time when an ideal set-up for its management is not available. The chances for a recurrence of hemorrhage are great. It is estimated that in more than sixty per cent it will recur.

The anxiety and fear of a recurrence of bleeding is like having the sword of Damocles hanging over one's head. I believe that bleeding from ulcer is an indication for surgery. In massive hemorrhage, immediate surgery, that is, as soon as shock is overcome, offers the best prognosis. With modern surgical technic, antibiotics, safe anesthesia, transfusions, etc., the mortality is lower than with expectant medical management, and the fear of recurrence is abolished.

I fully realize that this approach to the treatment of massive hemorrhage is radical and that it is not accepted by many medical men and surgeons at the present time, chiefly because confusion exists in evaluating published statistics which include all grades of bleeding. If, when speaking of hemorrhage from peptic ulcer, we differentiate massive hemorrhage from lesser amounts of blood loss, there would doubtless be a better understanding of the problems involved and more unanimity of opinion as to therapy.

MILESTONES IN THE DIAGNOSIS AND TREATMENT OF DIARRHEAL DISEASES*

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"Knowledge and Wisdom, far from being one
Have oft times no connexion; knowledge dwells
In heads replete with thoughts of other men;
Wisdom in minds attentive to their own.
Knowledge is proud that he has learned so much;
Wisdom is humble that he knows no more."

COWPER

Although diarrheal diseases have plagued humanity since the dawn of history, knowledge regarding their causes was not possible until the discovery of the microscope and the birth of bacteriology and protozoology. It required the wisdom of a humble Dutch bookkeeper, Anthony Van Leeuwenhoek[1] to mark the first milestone in the diagnosis and treatment of diarrheal diseases. His discovery of the method of grinding microscopic lenses, and then discovering the microscope, opened for him a new world of interest. He was so fascinated by the findings that he reported with great enthusiasm to the Royal Society of London each new microscopic picture. A total of 200 letters were received by the Society containing accounts of hundreds of discoveries. He described many types of protozoa in 1674, and in the following year, with improved lenses, described many types of bacteria. Interestingly enough he found *Giardia intestinalis* on microscopic examination of his own stool. Seventy years, almost three generations later, microscopes were first made available for commercial distribution. How different the time interval is today between a new discovery and its medical and therapeutic utilization!

Another 100 years passed before the golden age of the microbe hunters was ushered in, and microscopic findings were actually correlated to diarrheal diseases. The year 1859 was marked by Darwin's "Origin of Species" and Florence Nightingale's "Notes on Nursing". It was in this year that Lambl[2] at Prague found living amebae in the stools of a case of infantile diarrhea. Four years later, in 1863, Pasteur first established the relationship between bacteria and disease and in 1875, Lösch[3], in St. Petersburg, demonstrated this relationship when he found the *Entameba histolytica* in a case of chronic diarrhea. By injecting the fecal material rectally into four dogs he was able to reproduce the ulcers in the intestine of the animals and to recover the amebae from the ulcers. Robert Koch[4], in 1883 while in Alexandria and in India, Kartulis[5] while in Egypt, and in 1890

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Osler[6] in Baltimore, confirmed the findings of Lambl and Lösch to the end that a definite amebic type of diarrhea was clearly established.

It is of particular interest to recall that in the month of March 1890, Osler discovered amebae in material secured from an abscess of the liver of a patient with chronic diarrhea. He drew numerous pictures of the organisms especially of one ameba which on March 24th was watched for many hours. Two days later he wrote as follows to his friend Musser in Philadelphia: "We have been much excited over Kartulis' amebae which we have found in a liver abscess of a case of dysentery in a doctor from Panama. They are most extraordinary and striking creatures and take one's breath away at first to see these big amebae 10-20 times the size of a leucocyte crawling about in the pus. The movements are very active and in one case kept up for 10 hours. I get a fresh stock of pus from the drainage tube every day, so if you can run down some evening we could look for the creatures in the morning".

Fig. 1—Sigmoidoscopic aspirator in sigmoidoscope for purpose of aspirating fresh exudate under direct vision from mucosal lesion.

Thirteen years later, in 1903, Schaudin[7] was able to trace the life cycle of the human intestinal ameba. He thereby proved the existence of two types, the non-pathogenic E. coli and the pathogenic one E. histolytica.

We approach the next milestone in the year 1898. In this year the Curies isolated radium chloride, and in this same year Shiga[8], in Japan, isolated the bacillus dysenteriae in 34 of 36 cases suffering with acute severe diarrhea. This organism was found in the intestinal contents, in the visceral walls and mesenteric glands. It was the same organism in every case and showed uniform serum agglutination reactions. Further, he found that this bacillus was not present in the stools of patients suffering with other diseases, nor in those of normal men, and that when tested against the blood serum of such people it was not agglutinated. Thus a definite bacillary type of diarrhea was established. Shiga's findings were confirmed two years later by Kruse[9], Flexner[10] and Strong and Musgrave[11]. In 1902 Martini and Lentz[12] demonstrated serologically and by fermentation reactions that the bacilli of Shiga and Kruse differed from those of Flexner and Strong. In 1904 Duval[13] described another bacillus which he cultured from the intestine of a fatal case of diarrhea in an adult. This organism was extensively

studied by Sonne[14] in Denmark in 1913, and it now rightfully bears the names of both investigators as the Sonne-Duval bacillus.

Balantidium Coli was first described in 1857 by Malmsten[15], a Swedish investigator. He detected the protozoan in the stools of a patient and named it originally *Paramecium Coli*. Leuckart[16], in 1861, and Stein[17], in 1862, confirmed his findings. The latter investigator transferred the parasite to the *genus Balantidium* and called it *Balantidium Coli*.

The *Giardia intestinalis* was first seen by Leeuwenhoek, but was more accurately described by Lambl in 1859. It is of interest to remember that it is found in mammals and reptiles as well as humans. The infestation is more prevalent in children than in adults.

The *trichomonas hominis* was described by Davaine[18], in 1860, and Leuckart in 1879. *Chilomastix mesnili* was described by Wenyon and Alexeieff[19] in 1910. Their pathogenicity is of low grade and often questionable.

In 1915 Woodcock[20] discovered the cysts of Isopora in the feces of man and later in the same year Wenyon[21] also found them in the stools of a patient suffering with diarrhea. Connal[22], in 1922, accidentally infected himself with the cysts of *Isopora hominis*. After an incubation period of six days he suffered from diarrhea and proved their pathogenicity by finding the typical cysts in his own stool specimens.

Malarial diarrhea is frequently observed in severe infections with plasmodium falciparum. The severe diarrhea resembles true cholera unaccompanied by fever and associated with the passage of blood and mucus. The pathological findings were described in detail by Daniels[23], in 1901, and by Ross[24], in 1902.

Leishmanial diarrhea caused by *Leishmania donovani* is seen in severe cases of Kala-azar. Shortt, Smith, DeSilva and Swanienath[25], in 1929, were the first to demonstrate these parasites consistently in the stools of Kala-azar diarrhea.

Bilharzial diarrhea is caused by *B. Mansoni* and *B. Japonicum*. It was originally an African and Far Eastern disease respectively. The etiologic agent was first described in 1852 by Bilharz[26] and six years later by Weinland[27]. The discovery of the lateral-spined eggs usually in the feces suggested to Manson[28], in 1893, that there were two species of human schistosomes in Egypt, and therefore Sambon[29], in 1907, designated the hypothetical species with lateral-spined eggs, in honor of Manson as *Schistosoma mansoni*. Definite proof of the existence of two separate species, however, was not provided until Leiper[30], in the period from 1915 to 1918, carried out the life history studies which showed—(1) that there were two distinct species, one typically intestinal with lateral-spined eggs, and one typically vesical with terminal-spined eggs; (2) that these species were morphologically distinguishable; (3) that they required a different molluscan intermediate host; and (4) that infestation was acquired via the cutaneous route. The use of tartar emetic as a specific therapeutic in visceral schistosomiasis

was first advocated by McDonough[31], in 1918 and its efficacy actually demonstrated on a large scale by Christopherson[32] in the same year.

The visual examination of the rectum and sigmoid marks the next milestone. It dates back to Hippocrates[33] who described the first rectal speculum. There followed a period of 2,000 years during which no progress was recorded in the field of rectal instrumentation. In 1852 Sims[34] demonstrated a tube which he introduced into the rectum for rectosigmoidoscopic inspection. The illumination of the field consisted of a primitive alcohol lamp. This suggestive lead was lost for 43 years until in 1895, Kelly[35] revived the idea of rectal instrumentation and published a description of his proctoscope. It consisted simply of a tube and obturator. The inside of the tube was illuminated through a mirror fixed on the

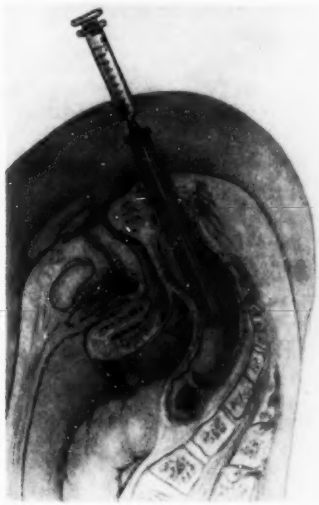

Fig. 2—Rectosigmoid aspirator in rectosigmoid for the purpose of aspirating a fecal saline suspension.

operator's forehead. Numerous changes have since been made in the construction of proctoscopes and sigmoidoscopes although actually the only basic change consists in the illumination of the tube by a small electric lamp.

A milestone denoting great progress in the study of diarrheal diseases was marked by the discovery of the x-ray by Roentgen[36], in 1895. Cannon[37] visualized the movements of the stomach three years later and the intestines in 1902, in animals, by using bismuth paste. The introduction of the Coolidge tube and Potter-Buckey diaphragm in 1913 lead to the study of the colon by means of the opaque enema, and the combined double contrast method advocated by Fischer[38] and later by Weber[39], and by Gershon-Cohen[40]. The applications of this miraculous new tool in the study of the causes of diarrheal diseases such as neoplasms,

inflammatory conditions and congenital anomalies of the small and large bowel were amazingly rapid.

The excellent work done by Bargen[41] of the Mayo Clinic in 1925 and since then, on the subject of ulcerative colitis, marks another landmark in the diagnosis and treatment of diarrheal diseases. His numerous experimental and clinical investigations not only aided the understanding of chronic ulcerative colitis but has promoted various technical and therapeutic measures so important in its management.

In 1925 Frei[42] made a notable discovery in the form of a specific skin test for the diagnosis of venereal lymphogranuloma. He found that sterile pus from a lesion after suitable dilution with sterile physiologic salt solution, inactivated by heating at 60° C. for a total of about three hours, and injected intradermally into the forearm of a patient with the disease would produce a pustule at least 6 or 7 mm. in diameter after 48 hours. Frei and Koppel[43] three years later in 1928 proved the relationship of diarrhea and rectal stricture with venereal lymphogranuloma.

The rapid development of Roentgen technic has made it possible to diagnose regional ileitis very early in its life history. Nonspecific granulomata of the small intestine were reported in the medical literature for many years. In 1813 Combe and Saunders[44] reported before the Royal College of Physicians of London, "A Singular Case of Stricture and Thickening of the Ileum". Fifteen years later in 1828 Abercrombie[45] discussed pathologic states of the ileum and reported cases very similar to regional ileitis. After a lapse of about 75 years numerous case reports began to appear in the English, German and American literature. The monumental work in this field belongs to Crohn[46]. His book on "Regional Ileitis" published in 1949 not only reports the existing literature but relates in a masterful style the life history, diagnosis and treatment of this baffling disorder.

One of the major complaints of patients suffering with gastrointestinal allergy, whether it be foods, drugs, pollens or bacteria, is diarrhea. Food allergy was noted as early as 75 B.C. It was Hippocrates who stated that "Cheese is not always tolerated by all men". Lucretius wrote, "One man's food is another man's poison". Gastrointestinal symptoms including diarrhea in allergic patients have been noted by many observers. Rowe[47], in 1931 reported 150 cases of gastrointestinal food allergy, 30 per cent of whom had complained of diarrhea and so-called "mucous colitis". The establishment of an allergic type of diarrhea has been admirably supported by the work of Andresen[48].

In 1934 the author[49] devised and reported in the *Journal of the American Medical Association*, an instrument, the "Rectosigmoid Aspirator" for the purpose of obtaining fresh saline suspensions of rectosigmoidal contents. The instrument is 8″ long and ¾″ in diameter. The sterilized aspirator is lubricated and inserted into the rectum for four or five inches. A 10 c.c. sterile syringe containing sterile saline is then attached and the saline injected into the bowel. Aspiration, injection

and reaspiration is then performed until a bloody, mucoid or fecal suspension of the desired concentration is obtained. The specimen is then ejected into a sterile test tube and sent to the laboratory for complete bacteriologic and protozoologic studies. It obviates the use of bedpans, paper or glass containers. The specimen is obtained fresh and under sterile precautions. It can be obtained any time during the day or night for diagnostic study or for purposes of instruction.

In the same year the "Sigmoidoscopic Aspirator" was devised and also reported by the author[50]. This instrument consists of a narrow tube, a 2 c.c. Luer-Lok syringe and a spiral spring. The spring is mounted over the piston of the syringe in order to facilitate aspiration with one hand while the other hand con-

Fig.3—Sigmoidoscopy—(With Kelly's sigmoidoscope in early 1900)

trols the sigmoidoscope. By means of this aspirator exudate can be obtained without outside contamination from the base of ulcerations directly under vision through the sigmoidoscope. It furnishes ideal material for diagnostic study. Both aspirators have been of inestimable value to the author in rapidly differentiating inflammatory from noninflammatory diarrheal disorders as well as bacterial infections from protozoan or metazoan infestations.

One of the great therapeutic milestones is the development of parenteral alimentation. The idea of parenteral administration of fluids and nutrition dates back to Harvey's[51] discovery of the circulation of the blood in 1616. The idea gained recognition in spite of many failures which were due mainly to infection,

to the inability to control blood coagulation, and to reactions due to ignorance of the blood groups and existence of pyrogens. In 1832 Latta[52] of Scotland was the first to use saline intravenously to replace lost water and salts in order to save hundreds of lives during an epidemic of cholera in England. Almost 100 years later, in 1915, only 37 years ago, Woodyatt[53] proved for the first time that glucose could be injected indefinitely in human beings at a rate of 0.9 gram per kilogram of body weight per hour without provoking glycosuria.

The science of nutrition developed rapidly during the past quarter of a century[54]. Foods were divided into water, electrolytes, proteins, fats, carbohydrates, and vitamins. Knowledge regarding the units into which these foods were reduced in the gastrointestinal tract, before absorption took place, was advanced during this period. Today these units are known. The parenteral replacement of water[55], electrolytes[56], amino acids[57], glucose, vitamins, plasma, blood, packed red cells and hormones[58] in the patient suffering with diarrhea is now a frequent and life-saving procedure. Nutritional failure which was a common finding in these patients only several years ago is now seldom encountered because of prompt parenteral alimentation.

Diarrheal diseases have been treated empirically for many centuries. Our famous fathers of medicine have thus achieved notable results with the psychogenic types of diarrhea. Although they were not aware of bacterial or other specific causes of diarrhea they fully realized the relationship of the emotions to diarrhea. Theirs was "shotgun" therapy. Etiologic diagnoses were unknown. All patients suffering with diarrhea were treated with the same mixture and the same psychosomatic approach. During the past quarter of a century more and more emphasis has been placed on psychosomatic factors in diarrheal diseases, so much so that patients with advanced ulcerative disease of the bowel are referred to psychiatrists and psychologists for therapy. The other day the author saw a boy, seven years of age, who was complaining of frequent bowel evacuations intermittently for over a year. His mother took him to many physicians who sent stool specimens to laboratories for examination. Because the reports were all negative for pathogens, the child was finally referred to a psychiatrist who fortunately refused to handle the patient until a more thorough bowel investigation was done. This patient was suffering with enormous fecal impactions in the rectum. No one examined the patient digitally per rectum, no one proctoscoped the child. Although psychogenic diarrhea is of frequent occurrence no such diagnosis should ever be attempted, and no patient should be referred for psychiatric aid before a complete history, physical, rectal digital, sigmoidoscopic, bacteriologic and x-ray investigation is carried out.

An important therapeutic milestone was the introduction of emetine as a remedy for dysentery by Bardsley[59], of Manchester, in 1829, thirty years before the E. histolytica was described by Lambl, and almost fifty years before amebic disease was suggested by Losch. The drug was first derived from ipecacuanha by Pelletier[60] as early as 1817. Almost 100 years later, in 1911, Vedder[61] demon-

strated the lethal action of emetine upon the pathogenic ameba. The following year Sir Leonard Rogers[62] established the clinical effectiveness of emetine in amebic diarrhea. This drug has stood the test of time. Today it is still one of our basic antiamebic drugs.

In 1936 Long[63] introduced the sulfonamide drugs in the United States. His enthusiasm for the experimental and clinical studies on Prontisil and Sulfanilamide was stimulated by the successful reports on streptococcal infections at the London Lying-In Hospital by Colebrook[64] and his team. This prompted Marshall[65], Bargen and numerous other clinicians to use the sulfa drugs in diarrheal diseases. Neo-prontisil, Sulfadiazine, Sulfaguanadine, Succinyl-Sulfathiazole, Sulfathaladine and Thalamyd were all found to be beneficial in selected cases of bacterial diarrhea.

The antibiotic drugs have, in may respects, revolutionized the study and management of infectious diarrheal diseases. Their large spectrum of activity and their usefulness against pathogenic bacteria, viruses and even protozoa is one of the most amazing discoveries of our times. The use of Penicillin, Streptomycin, Aureomycin, Chloromycetin and Terramycin, separately and in combination, has practically eliminated the serious complications of diarrheal diseases, and has greatly reduced the need for surgical intervention. Combined therapy with some of the sulfa drugs such as Sulfadiazine has been found to be effective in the acute critical stages of diarrheal diseases especially those of ulcerative colitis and ulcerative regional enteritis. Also, prophylactic antibiotic therapy, when fully developed, promises to be most useful in the prevention of epidemics or even relapses in chronic infectious diarrheal diseases.

It is heartening to feel that surgical intervention in diarrheal disease in the form of ileostomy, ileocolostomy, partial resections of the bowel, and colectomy is less dangerous today. The advances made in gastrointestinal surgery during the past two decades mark a milestone in the therapy of diarrheal diseases. Although colectomy in chronic ulcerative colitis is far from the ideal treatment it is nevertheless indicated in a very few well selected cases[66]. The occurrence of diarrhea following faulty gastrointestinal anastamoses or resections is now rare due to improved surgical technic.

The books on "Dysenteric Disorders" by Manson-Bahr[67] on "Diarrheal Diseases—Diagnosis and Treatment" by the Author[68] and "Bacillary Dysentery Colitis and Enteritis" by Felsen[69] have served to focus attention on this old and highly neglected field. These books have introduced the etiologic approach and thus established the treatment of diarrheal diseases on a more scientific foundation.

Time does not permit the inclusion of many important advances. They will be found in the "Atlas of Diarrheal Diseases" a new book in preparation. In conclusion the author has tried to trace the development of the field of diarrheal diseases from the birth of bacteriology through the discoveries of the various

pathogenic bacteria, protozoa, metazoa and other etiologic agents. An attempt was made to present the major diagnostic and therapeutic discoveries which may be of interest to the physician in the management of these disorders.

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Discussion

Dr. Hyman I. Goldstein (Camden, N. J.):—Dr. Fradkin's presentation is really a thrillingly interesting experience and I must comment on it.

We have had a real treat listening to such an excellent résumé of the story of the diarrheal diseases. I could not resist the temptation, Mr. Chairman, to ask for the privilege of discussing this paper because it is not often that we have papers of an historical nature. We did have a nice historical presentation last night by our friend, Dr. I. Snapper, and he did very well until he came to Phila-

delphia in his story, and then he was quite confused about the medical faculty of the first medical school (1765) of the American Colonies, The University of Pennsylvania—and the clinical teaching at the Pennsylvania Hospital begun in 1767!

Dr. Fradkin mentioned a number of interesting historical events. It might be of interest to him and to the audience, about the diarrhea of the Jews when they made their exodus from Egypt and demanded shovels to cover up the excreta with dirt, to prevent the spread of the diarrheal disease at that time. That is of Biblical origin, and the Bible was compiled ca. 1300 B.C. Augustus Caesar, who lived to a ripe old age, and had an adopted son who was anxious to get the royal chair, suffered from attacks of diarrhea. It wasn't psychogenic—because at autopsy (after death) they found an abscess of the liver—perhaps the dysentery caused an amebic abscess—or was it an hydatid cyst and abcess?

Dr. Fradkin mentioned Combe and Saunders, and their report of ileitis in 1813. It was I who discovered this case report some years ago. The report was read on July 5, 1806. The doctor mentioned Abercrombie and his report. I also discovered this report some years ago. This was in a girl about thirteen years old. Abercrombie saw the patient in 1814 and published it in his book in 1828. In 1810, David Hosack, for whom "David Hosack Hall" was named here in the New York Academy of Medicine, had a patient that Dr. John Wakefield Francis, a pathologist of the old faculty of Kings' College reported in 1810. This is the first case in medical literature in which the patient not only had regional enteritis but it was also associated with a Meckel's diverticulum, and illustrated with a beautiful plate, the first plate of this condition in the literature!

It is interesting to note, that it is one hundred years since Sims introduced his tube in 1851, and that it is exactly one hundred years ago that Doctor Récamier died (1852).

We use the term "metastasis" and we know that cancer will metastasize to distant points, but I don't believe there is a man in the audience—and this is not by way of criticism, but to emphasize the tragedy of medicine and how we forget these men—who recalls that it was Récamier who had a patient with cancer of the breast, and later this woman developed a cerebral "accident" (in 1828) and he clinically recognized that this was due to "metastasis" from the *breast cancer!* This was the first time in the history of medical literature that the term "metastasis" was used, and it was coined by Récamier, and the case was clinically diagnosed correctly as "metastasis"!

It is not generally known that Marcel Donatus, in the sixteenth century diagnosed carcinoma of the rectum. He used a wax wick to locate it, and with blood on that, diagnosed cancer of the rectum—and, it was a carcinomatous lesion diagnosed with the wick, proved at autopsy!

Of course, the gentlemen who go before the state boards and specialty boards know what "psychogenic diarrhea" is.

Trichinosis might be mentioned because a Philadelphian, Joseph Leidy, first discovered trichina in the hog in 1846. Thomas Sydenham, the English Hippocrates, in the seventeenth century wrote quite a number of paragraphs on diarrheas, and probably observed ulcerative colitis, and the dysenteries.

Jean Fernel, born in 1497 and died in 1558, published *the first book* called "Patologia", and in his "Medicina", reported a case of what apparently was an appendiceal abscess, but with "thickening" of the ileocecal area and the ileum. This may have been a case of regional ileitis with an appendiceal abcess!

This may hold true in Mestivier's case (1757) too. In closing, since Dr. Fradkin mentioned "antibiotics", I might tell you that in 1872-1876, John Tyndall, a microbiologist, in his little book (1880; 1881), *Relation of Foreign Particles in the Air to Infection and Putrefaction*, reported his experiments with various culture media, and observed some tubes that apparently were clear, with the sediment in the bottom, and other tubes flourishing with live organisms. He states that the sediment in the clear tubes consisted of dead and dormant bacteria, *caused by Penicillium glaucum in the tubes!*

Can you imagine the millions of lives which might have been saved had someone followed these observations and repeated these experiments on animals, and then on humans during the past 76 years?

PROBLEMS IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE*

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and

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The differential diagnosis of jaundice has been facilitated by improved clinical acumen, the introduction of better biochemical liver function tests and wider use of aspiration biopsy of the liver. To evaluate accuracy in the diagnosis of jaundice, case histories of 438 unselected patients with clinical jaundice and serum bilirubin of more than 2 mg. per cent observed in the Jersey City Medical Center between 1947 and 1952 have been reviewed.

Clinical evaluation consisted of history, physical examination, and routine laboratory studies. Special laboratory studies such as reticulocyte counts, the Coombs test[1] duodenal drainage and cholecystography and cholangiography were performed in selected patients. Biochemical liver function studies, selected individually, included serum bilirubin[2], urine and fecal bile[3], urine and fecal urobilinogen[4], bromsulfalein excretion[5], serum alkaline phosphatase[6], serum cholesterol and esters[7], serum albumin and globulin[8], cephalin-cholesterol flocculation[9], thymol turbidity[10], glycogen storage[11], intravenous galactose tolerance[12], and prothrombin time response to Vitamin K[13]. Liver biopsies were performed with the Vim-Silverman needle without complications[14].

Jaundice was divided into prehepatic, hepatic and posthepatic varieties[15]. Prehepatic jaundice results from acceleration of the production of bilirubin-globin beyond the disposal capacity of the reticuloendothelial system. Hepatic jaundice is due to injury of liver cells which interferes with the separation of bilirubin-globin or decreases the excretion of bilirubin. Posthepatic jaundice is due to obstruction to bilirubin outflow (Fig. 1). One hundred and twenty-four patients had prehepatic jaundice, 179 had hepatic jaundice, 104 had posthepatic jaundice and 31 had combinations of these types of jaundice.

Confusing clinical features, difficulties in interpreting biochemical and histological studies, and the presence of more than one cause for jaundice led to diagnostic errors. An accurate diagnosis was made on clinical features and biochemical function study in 105 (84.8 per cent) patients with prehepatic jaundice, 107 (59.8 per cent) patients with hepatic jaundice, 83 (79.8 per cent) patients with posthepatic jaundice and 12 (38.6 per cent) patients with two causes of jaundice. Needle biopsy of the liver was employed as an adjunct in 10 (8 per cent) patients with prehepatic jaundice, 44 (24.6 per cent) patients with hepatic jaundice, 15 (14.4 per cent) patients with posthepatic jaundice and 8 (25.8 per cent) patients with two causes of jaundice. Prolonged observation with surgical

*From the Department of Medicine, Jersey City Medical Center.

exploration or postmortem examination established a diagnosis in 9 (7.2 per cent) patients with prehepatic jaundice, 28 (15.6 per cent) patients with hepatic jaundice, 6 (5.7 per cent) patients with posthepatic jaundice and 11 (35.6 per cent) patients with combination causes of jaundice.

Clinical Features

The symptom-complex and physical signs classified by age groups permitted a correct decision as to the cause of jaundice in 75 per cent of the patients. Signs and symptoms were of considerable help individually but were of greater value collectively. The diagnosis of hemolysis was apparent when the patient developed sudden jaundice with chills and fever following transfusion. Primary liver injury was suggested in the alcohol user with poor dietary habits. Gallstones were considered in the patient with previous biliary colic who developed jaundice and right upper quadrant pain. All except one of 76 newborn infants* had prehepatic icterus. Hepatic jaundice due to viral hepatitis (I.H.), occurred

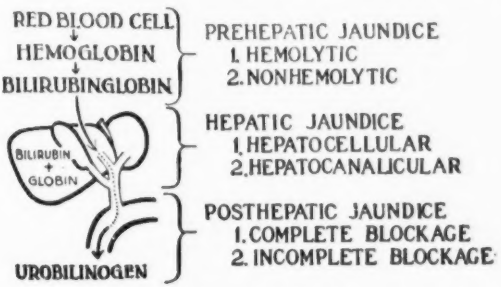

Fig. 1–Causes of jaundice.

predominantly in the age groups 12 to 30 and that due to portal cirrhosis between 40 and 60. Most of the patients with posthepatic jaundice were over 50 years of age. Viral hepatitis (S.H.), following injections or transfusions, occurred in each of the groups. This decreased the value of age in deciding the cause of jaundice.

History of exposure to hepatotoxic agents often furnished a rapid clue to diagnosis. Symptomatology was frequently unreliable. Biliary colic was the most specific symptom occurring in 41 (39.4 per cent) of the group with posthepatic jaundice, in only 7 (3.9 per cent) of those with hepatic jaundice, and in none of those with prehepatic jaundice. Symptoms of anemia were present in 22 (17.7 per cent) patients with prehepatic jaundice, 16 (8.9 per cent) patients with hepatic jaundice and 12 (11.5 per cent) patients with posthepatic jaundice. Gastrointestinal disturbances were present in 4 (3.2 per cent) patients of the prehepatic group, 153 (85.4 per cent) patients of the hepatic group, and 82 (78.9 per cent)

*Reviewed at the Margaret Hague Maternity Hospital, Courtesy of Dr. S. A. Cosgrove.

patients of the posthepatic group. Symptoms due to fluid retention occurred in 4 (3.2 per cent) patients with prehepatic jaundice, 59 (32.9 per cent) patients with hepatic jaundice, and 6 (5.7 per cent) patients with posthepatic jaundice.

Physical findings were more helpful. The presence of a palpable gallbladder allowed a definite diagnosis of posthepatic jaundice in 8 (7.6 per cent) patients in the posthepatic group. Spider angiomata and evidence of collateral circulation were usually specific for hepatic jaundice. Spider angiomata were seen in 36 (20.1 per cent) patients with hepatic jaundice, only 2 (1.9 per cent) patients with posthepatic jaundice and none with prehepatic jaundice. Collateral circulation was limited to the hepatic group and was present in 25 (13.9 per cent) of these patients.

Liver tenderness, hepatomegaly and splenomegaly were suggestive of hepatic jaundice. Liver tenderness was present in 32 (17.8 per cent) patients of the hepatic group, in 3 (2.4 per cent) patients of the prehepatic group and in 5 (4.7 per cent) patients of the posthepatic group. Hepatomegaly was present in 136 (85.9 per cent) patients with hepatic jaundice, 17 (14.5 per cent) patients with prehepatic jaundice and 29 (27.8 per cent) patients with posthepatic jaundice. Splenomegaly occurred in 36 (20.1 per cent) patients with hepatic jaundice, 15 (12.0 per cent) patients with prehepatic jaundice and 3 (2.8 per cent) patients with posthepatic jaundice.

Biochemical Function and Other Laboratory Studies

Biochemical study of liver function yielded a correct diagnosis of the general cause of jaundice in 83 per cent of the patients in this series (Table I). Errors resulted from reliance on one or two tests or the nonspecificity of biochemical studies. Adequate excretory tests were ordered in most problem cases, but metabolic function evaluation was limited to protein studies in many instances. Cholesterol and carbohydrate studies increased the diagnostic value of the biochemical profile.

Studies of bilirubin metabolism offered the simplest means of differentiating jaundice. Fractionation of serum bilirubin was helpful in supporting the diagnosis of hemolytic jaundice, but was of limited value in differentiating between biliary obstruction and hepatocellular disease. This test is influenced both by the concentration of bilirubin in the serum and by chemical-physical properties of bilirubin-globin[16].

Urine and fecal bile and urobilinogen determinations were useful in uncomplicated prehepatic and posthepatic jaundice. The administration of antibiotics, which altered the reduction of bilirubin by intestinal flora[17], made urobilinogen studies less useful. Failure to employ fresh urine in testing for urobilinogen also led to erroneous conclusions.

The serum alkaline phosphatase level was valuable in the diagnosis of posthepatic jaundice. Enzyme levels of more than 10 Bodansky units were obtained

in 91 per cent of patients with uncomplicated posthepatic jaundice. The level was normal in prehepatic jaundice and variable in hepatic jaundice. High phosphatase levels occurred in cholangiolitic hepatitis and metastatic malignancy. The value of this test diminishes in anemia, malnutrition, states of bone growth or reabsorption. One infant with congenital atresia of the bile ducts showed a normal alkaline phosphatase level. Bromsulfalein excretion was of little value in differential diagnosis.

TABLE I

EXPECTED LABORATORY FINDINGS IN UNCOMPLICATED JAUNDICE*

	Prehepatic	Hepatic	Posthepatic
Reticulocyte Count	Over 5%	1-3%	1-3%
Prompt Reacting Bilirubin	.03-0.5 mg.%	0.5 mg. %	0.5 mg. %
Delayed Bilirubin	> 0.5 mg.	> 0.5 mg.	0.3-0.5 mg.
Bile in Urine	0	0-4+	1-4+
2 Hour Urobilinogen in Urine	> 1.5 Eh. U	Variable	0-0.65 Eh. U
Alkaline Phosphatase	0-5 B. U	0-15 B. U	5-30 B. U
Total Cholesterol	180-250 mg. %	Variable	250 mg. %
Cholesterol Esters % of Total	60-70%	< 50%	60-70%
Serum Albumin	3.5-5.0 gm. %	3.5-5.0 gm. %	3.5-5.0 gm. %
Serum Globulin	1.5-2.5 gm. %	1.5-2.5 gm. %	1.5-2.5 gm. %
Cephalin Flocculation	0-1+	2+-4+	0-1+
Thymol Turbidity	0-4.0 U	> 4.0 U	0-4.0 U
Galactose Tolerance	< 5 mg. % retained in 75 minutes	> 5 mg. % retained in 75 minutes	< 5 mg. % retained in 75 minutes
Glycogen Storage Blood Sugar Rise	40-60 mg. % rise	< 40 mg. % rise	40-60 mg. % rise
Prothrombin Time Response to Vitamin K	Ret. to Normal	No Response	Ret. to Normal
Needle Biopsy	Bile Stasis	Hepatocellular Changes	Bile Stasis

*Modification of these values is necessary in the newborn infant[28].

Estimation of serum cholesterol and the ester fraction was helpful. The serum cholesterol was elevated in uncomplicated posthepatic jaundice, but hypercholesterolemia was also present in hepatic jaundice. Liver disease together with familial hypercholesterolemia, nephrosis, diabetes, pregnancy, or hypothyroidism limited the value of this test. Jaundice complicated by anemia, hyperthyroidism or malnutrition which reduced the total cholesterol, presented a similar problem. The ester fraction of serum cholesterol provided more help because a

level less than 60 mg. per cent always indicated hepatic damage, although it did not define the mechanism.

Plasma protein studies were not helpful in deciding the cause of jaundice. Patients with jaundice did not show protein alterations early in their course; later abnormal protein patterns occurred in each group. Flocculation tests, based on the presence of abnormal proteins, were of considerable importance in recognizing hepatic jaundice. The cephalin flocculation was more valuable than the thymol turbidity. These two tests measure different protein variations[18], and together provided information not available with either single test. Normal prothrombin response to Vitiman K suggested posthepatic jaundice although some patients with intrahepatic jaundice had normal responses.

The galactose tolerance test was of considerable help in differentiating hepatic and posthepatic jaundice. The intravenous technic eliminates gastrointestinal and renal factors. Icterus due to acute hepatic injury was accompanied by intolerance to infused galactose. Uncomplicated posthepatic jaundice was associated with normal galactose tolerance. The glycogen storage test was more useful as a therapeutic guide, although it was helpful in diagnosis with acute viral hepatitis. Carbohydrate tests were the only metabolic studies indicating hepatic damage in some instances.

Needle Biopsy of the Liver

Aspiration biopsy of the liver was the most effective means of differentiating hepatic jaundice from posthepatic jaundice or prehepatic jaundice and the only method of deciding the specific cause of hepatic jaundice. Its chief detraction is the possibility of bile peritonitis following this procedure in jaundiced patients. Abnormal bleeding tendencies which often accompany hepatic jaundice is a further limiting factor. Biopsy was performed on 84 patients in this series who presented a problem in diagnosis.

Information provided by the biopsy was related to finding the portal area, central area, both of these areas, or neither in the histologic sections. A diagnosis of posthepatic jaundice was made when the biopsy showed (a) biliary stasis with bile casts and intracellular bile granules without cellular changes; (b) biliary stasis with proliferation of Kupffer cells, bile ducts and periportal connective tissue characteristic of biliary cirrhosis; (c) biliary stasis with periportal and perilymphatic inflammation characteristic of cholangitis[19]. A diagnosis of hepatic jaundice was made when the characterstic histological features of viral hepatitis, toxic hepatitis, portal cirrhosis, multiple nodular hyperplasia or central congestion were present. Frequently necrosis was a conspicuous feature of the pathological picture. Viral hepatitis was diagnosed by disorganization of the lobular pattern, focal intralobular and periportal collections of inflammatory cells and active regeneration of liver cells with and without acidophilic coagulative necrosis. Toxic hepatitis was characterized by coagulation necrosis, a neutrophilic

inflammatory reaction with moderate fatty changes. A diagnosis of portal cirrhosis (diffuse hepatic fibrosis) was based upon the presence of periportal fibrosis with bile duct proliferation and pseudolobulation with or without hyaline necrosis, fatty changes or lymphocytic infiltration. A diagnosis of multiple nodular hyperplasia (postnecrotic scarring) was based on nonreactive fibrosis, demonstration of the skeleton of a pre-existing lobule and proliferation of bile canaliculi. Central necrosis was diagnosed by the presence of dead cells or absence of hepatic cells along with condensation of the reticulum around the central vein[15]. Liver biopsy was decisive in 76 (90.5 per cent) patients, was not helpful in 6 (7.1 per cent) patients and led the clinician astray in 2 (2.4 per cent) patients. It was not helpful in patients with cholangiolitic hepatitis with bile stasis as the only abnormality, and exploratory surgery was necessary to differentiate this type of jaundice from extrahepatic obstruction. Biopsies were confusing in two patients with inflammatory reactions secondary to extrahepatic biliary obstruction.

Combination Causes of Jaundice

Thirty-one patients with two mechansims contributing to jaundice constituted diagnostic problems[20] despite careful clinical evaluation, complete biochemical study and needle biopsy of the liver. These combined causes consisted of hepatic jaundice and prehepatic jaundice in 13 instances, hepatic jaundice and posthepatic jaundice in 12 instances and posthepatic jaundice and prehepatic jaundice in 4 instances.

The diagnosis of hepatic and prehepatic jaundice was based on clinical, biochemical and histologic evidence of liver disease and increased red blood cell destruction. In this group there were 3 patients with hemolysis due to sickle cell disease, 6 patients with chronic circulatory congestion showing hepatomegaly who suffered pulmonary infarction, 1 patient with liver disease and isohemolysis, and 2 patients exposed to chemical toxins.

Jaundice resulting from hepatic and posthepatic mechanisms was often difficult to classify. Five patients were observed with active liver disease and jaundice who also had superimposed posthepatic disease. Common duct stone complicated active portal cirrhosis in 3 of these patients, 1 patient had carcinoma of the head of the pancreas, and 1 patient developed primary liver cell carcinoma. The diagnosis was more difficult because the patients were seen in a late stage of hepatic insufficiency. The following case history is illustrative:

Case 1:—W. S., a 54 year old laborer, was hospitalized in 1947 because of alcoholism. Clinical and biochemical studies led to a diagnosis of portal cirrhosis. He was followed in the Clinic but continued to drink whiskey each day. In 1950, a needle biopsy confirmed the diagnosis of portal cirrhosis. Biochemical liver function studies at this time were similar to previous studies and showed a moderate hyperbilirubinemia, normal alkaline phosphatase, hyperglobulinemia, 4+ cephalin flocculation and poor glycogen storage. In 1951, he was hospitalized

because of a sudden increase in icterus. Biochemical studies suggested an obstructive element (Table II). Needle biopsy showed bile stasis in addition to cirrhosis (Fig. 1). Exploratory operation revealed an inoperable carcinoma of the head of the pancreas. Postmortem examination confirmed the clinical and preoperative diagnoses.

Seven patients with posthepatic jaundice sustained marked biochemical changes and permanent anatomical damage from prolonged biliary obstruction. Five of these patients had recurrent cholangitis due to common duct stones. This led to multiple liver abscesses in 1 patient and biliary cirrhosis in 4 patients. Two infants with bile duct atresia developed biliary cirrhosis. Recognition of the basic etiology was often difficult due to clinical and biochemical evidence of hepatic insufficiency.

TABLE II

OBSTRUCTIVE JAUNDICE SUPERIMPOSED ON PORTAL CIRRHOSIS, CASE 1.

	Oct. 1947	March 1949	March 1950	March 1951
S. Bil.	0.3 mg. %	0.7 mg. %	2.1 mg. %	31.0 mg. %
B.S.P.	30%	16%	25%	80.0%
Alk. Phos.	3.4 U	4.2 U	4.5 U	19.2 U
S. Cholesterol	250 mg. %	393 mg. %	380 mg. %	465 mg. %
Chol. Esters	110 mg. %	253 mg. %	240 mg. %	110 mg. %
S. Alb.	3.42	3.6	3.5	3.5
S. Glob.	3.80	4.1	4.1	4.0
Ceph. Flocc.	4+	4+	4+	4+
Thymol Turb.	5.0	4.0	4.0	4.0
Galactose	15	10	—	10

Of the 5 patients with combined posthepatic and prehepatic jaundice, 1 had carcinoma of the ampulla of Vater with isohemolysis, 3 had carcinoma of the head of the pancreas with pulmonary embolization and infarction, and 1 had chronic hemolytic jaundice with common duct obstruction from gallstones. Clinical features coupled with serial biochemial studies provided the clue to the presence of these two mechanisms.

CHOLANGIOLITIC DISEASE

A major difficulty in diagnosis was encountered in 6 patients with hepatic jaundice who showed impairment of excretory functions without metabolic changes. This is often characteristic of the liver injury associated with arsenic and other heavy metal poisoning[21], and in some instances of viral hepatitis[22]. Occasionally, it may be seen in nonobstructive bacterial cholangitis[23]. Such patients

generally deserve surgical exploration unless there is a clear history of exposure to hepatotoxins. Some of these patients subsequently develop metabolic changes, most have obstructive features alone. Typically, patients have hypercholesterolemia, hyperphosphatemia, biliuria and intense pruritus[24]. The following case history is illustrative:

Case 2:—M. F., a 41 year old housewife, was well until one month before hospitalization when upper abdominal discomfort appeared. Atabrine was administered because of intestinal giardiasis. After medication, she became jaundiced and had chills, fever, nausea, vomiting, right upper quadrant pain, and severe itching of the skin. Examination revealed jaundice with no palpable masses. Liver function studies revealed a serum bilirubin of 22 mg. per cent, urine bile 4+, absent urine urobilinogen, alkaline phosphatase 32 units, total cholesterol 427 mg. per cent, cholesterol esters 219 mg. per cent, serum albumin 4.0 mg. per cent, serum globulin 3.5 gm. per cent, cephalin flocculation negative, and

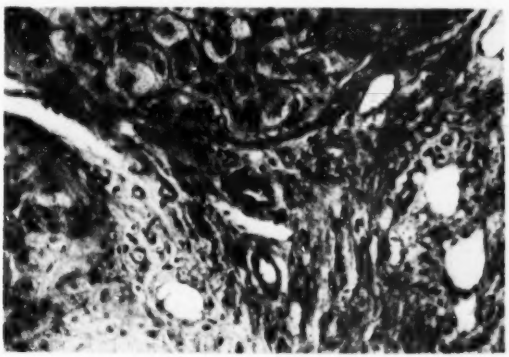

Fig. 2—Portal cirrhosis with bile stasis.

thymol turbidity 2.0 units. A needle biopsy of the liver revealed bile stasis without cellular abnormalities (Fig. 2). Jaundice remained unchanged and one month after admission, surgical exploration and a postoperative cholangiogram revealed no abnormalities. Her jaundice gradually subsided.

Secondary Diagnostic Problems

After jaundice has been classified as prehepatic, hepatic or posthepatic, the equally formidable task of deciding specific cause often remains. Sixty patients or 13.6 per cent of the total group presented secondary diagnostic problems; 9 of the prehepatic group, 15 of the hepatic group and 36 of the posthepatic group. Of the 124 patients with prehepatic jaundice, 84 had nonhemolytic disease and 40 had hemolytic disease (Table III).

Specific cause was difficult to evaluate in 5 cases in the nonhemolytic group. Further observation established that 2 patients had a congenital defect in

accepting bilirubin-globin[25], and 3 patients had hematomas. The interesting diagnostic problem in this group was presented by a patient developing jaundice following cholecystectomy. This resulted from an intraabdominal hematoma which later was evacuated at a second operation.

In the hemolytic group, a diagnosis was not readily made in 4 (10 per cent) patients. These diagnoses involved hematological studies[26]. Eleven patients had hemolytic jaundice due to intracorpuscular defects, 29 had jaundice due to extracorpuscular abnormalities.

The precise differential diagnosis of hepatic jaundice was frequently possible only after histologic studies. When feasible, a complete diagnosis was made to include clinical grade, biochemical function and pathological classification. Seventy-one patients of this group had hepatitis, 90 had cirrhosis, 14 had fatty

TABLE III

CAUSES OF PREHEPATIC JAUNDICE

A. Nonhemolytic:		
1. Congenital Defect		2
2. Pulmonary Infarction		22
3. Hematomas		3
4. Physiologic of Newborn		57
B. Hemolytic		
1. Intracorpuscular Defects:		11
a. Congenital Hemolytic Jaundice	2	
b. Sickle Cell Anemia	7	
c. Mediterranean Anemia	2	
2. Extracorpuscular:		29
a. Immune Body Reactions:		
Transfusion	10	
Erythroblastosis	7	
b. Infections, Chemical, Physical Agents, Poisons	6	
c. Secondary Hemolytic Anemia in Malignancy, Liver Disease	6	

livers with varying degrees of fibrosis, and 4 had liver abscess. Problems in determining specific cause were present in 15 (14.4 per cent) patients of this group.

Although posthepatic jaundice is a surgical problem, it was desirable to know the nature of the lesion before operation. The specific cause of posthepatic jaundice was not determined before exploration in 36 patients or 34.6 per cent of this series. Six patients were found to have stricture, 45 neoplastic obstruction and 53 calculous disease. Complete obstruction in the newborn or previous biliary surgery supported the diagnosis in patients later shown to have stricture. Neoplasms were suspected in 9 patients shown to have calculi. A preoperative diagnosis of neoplasm was made in 6 patients because of an x-ray change in the duodenal mucosa, and in 12 patients on clinical features. In 27

patients, the diagnosis was entertained on statistical probability. Duodenal drainage and exfoliative cell study increased the accuracy of preoperative diagnoses[26]. Incomplete obstruction to bile outflow and signs and symptoms of gallstones permitted a positive diagnosis of calculous disease in 44 patients (83 per cent).

The cause of posthepatic jaundice was elusive even during surgery in many instances. The lesion was often difficult for the surgeon to locate because of old adhesions disturbing anatomical relationships. If the gallbladder appeared normal and the bile ducts were patent, the possibility of tumor of the ampulla of Vater, intrahepatic stones, or a tumor involving the angle of the hepatic ducts producing intermittent obstruction was considered. An attempt was made to exclude a lesion of the papillae of ampulla of Vater by cholangiography[27] or opening the duodenum in such patients. The diagnosis of intrahepatic stones or tumor was occasionally made with cholangiography. The difficulty inherent in these patients is illustrated by the following case history:

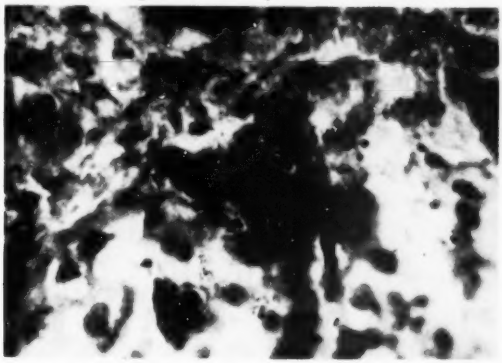

Fig. 3—Marked bile stasis in cholangiolitic hepatitis.

Case 3:—J. M., a 57 year old painter, was well until 3 months before hospitalization when he noted onset of weakness, malaise, anorexia, nausea and painless jaundice. He had used carbon tetrachloride as a cleaning fluid. Physical examination revealed icterus and hepatomegaly. A biochemical liver profile showed a serum bilirubin of 23.2 mg. per cent, alkaline phosphatase 40 units, serum cholesterol 750 mg. per cent, cholesterol esters 300 mg. per cent, serum albumin 2.04 gm. per cent, serum globulin 4.16 gm. per cent, thymol turbidity 2.0 units, cephalin flocculation 1+. There was bilirubinemia and urobilinogen was present in 1:20 liter in the urine. A diagnosis of extrahepatic obstructive jaundice was made and an exploratory operation performed. The gallbladder and pancreas were normal. Bile ducts were patent. The liver was large and a biopsy was taken from an abnormal area. The biopsy showed much scar tissue and bile duct proliferation suggesting postnecrotic scarring. The patient gradually went downhill and expired. Postmortem examination revealed carcinoma of the intrahepatic bile ducts with marked spread to the posterior surface of the liver.

Therapeutic Aspects

The diagnosis of prehepatic, hepatic or posthepatic jaundice is important for treatment. Twenty-eight (8.6 per cent) patients in this series were erroneously handled because of an error in primary diagnosis. Eleven patients with hepatic or prehepatic jaundice were operated on, while surgery was delayed from one to three weeks in 17 patients with posthepatic icterus.

Surgery should be avoided in patients with hepatic jaundice. Healthy subjects without liver function changes usually show biochemical and histological alterations following anesthesia and surgery[28]. These changes added to the liver showing previous injury may prove fatal or lead to chronic liver disease.

Patients with hepatic jaundice subjected to operation made poor responses in the immediate postoperative period. Two patients had a long stormy postoperative period. Diagnostic errors resulted from lack of adequate biochemical studies or clinical observation in 5 patients, from the nonspecificity of laboratory procedures in 3 patients, and from the similarity of cholangiolitic hepatitis to posthepatic jaundice in 3 patients.

Delay in operative relief of obstructive lesions leading to jaundice is also bad. Patients with posthepatic jaundice who were treated for long periods without surgery showed progressive decrease of liver function. Diagnostic errors in this group resulted from inadequate biochemical or clinical observation in 3 instances, confusion in laboratory study in 6 instances and hepatocellular changes secondary to biliary obstruction producing the clinical, biochemical and histological abnormalities characteristic of hepatic jaundice in 7 instances.

Patients with jaundice were kept at complete rest in bed and treatment has included a high carbohydrate intake and Vitamin K parenterally during the period of study. This program has improved the general status of patients in each of the groups while laboratory studies were being obtained.

Summary and Conclusions

1. The clinician is still confronted with many difficulties when his patient has jaundice. Problems in diagnosis arise because clinical features of the disease may be confusing, biochemical liver function tests and other laboratory procedures are not specific, aspiration biopsies of the liver are occasionally difficult to interpret and more than one cause for jaundice may be present.

2. Clinical features permitted a correct differentiation between prehepatic, hepatic and posthepatic jaundice in 75 per cent of 438 patients. Signs and symptoms were of considerable help individually and collectively. The age of the patient and symptoms incident to a hematological abnormality were important clues in the prehepatic group. A history of exposure to hepatotoxins, hepatic tenderness and spider angiomata were of value in the hepatic group. Biliary colic and a palpable gallbladder were helpful findings in the posthepatic group.

3. Biochemical liver function tests permitted a diagnosis of the cause of jaundice in 83 per cent of the patients. Each of the available tests was found to have limitations and was more helpful when used with other studies. Fractionation of serum bilirubin was only helpful in the diagnosis of prehepatic jaundice. A combination of the serum alkaline phosphatase and cephalin flocculation was of greatest value in differentiating hepatic and posthepatic jaundice. Cholesterol esters, galactose tolerance and quantitative urine bile and urobilinogen were also valuable.

4. Needle biopsy of the liver was the most effective method of differentiating problem cases of jaundice and deciding the specific mechanism of hepatic jaundice. In selected problems it was diagnostic in 91.3 per cent patients, was not helpful in 7.1 per cent patients, and led the clinician astray in 2.4 per cent patients. Biopsy was not helpful in differentiating cholangiolitic hepatitis from posthepatic jaundice and exploration was necessary with persisting jaundice. Biopsy was confusing in 2 patients with marked hepatocellular changes secondary to biliary obstruction.

5. Combinations of prehepatic, hepatic and posthepatic mechanisms for jaundice were present in 31 patients and led to considerable diagnostic difficulty. Constant cognizance of this possibility and acquaintance with those states in which it is encountered facilitates the recognition of two causes contributing to jaundice.

6. Problems in deciding the specific mechanism leading to jaundice were present in 9 patients with prehepatic jaundice, 15 patients with hepatic jaundice and 36 patients with posthepatic jaundice. Hematological studies were essential in the prehepatic group, needle biopsy in the hepatic group and duodenal drainage and smears in the posthepatic group. The problem of specific cause continued at the time of surgery in the post hepatic group and often required cholangiography.

7. Diagnostic errors led to incorrect therapy in 28 or 6.5 per cent of the patients. Errors, attributed to inadequate biochemical studies, inadequate clinical observation, and inherent difficulties were associated with an increased morbidity and mortality. These errors may be reduced to a minimum in problem patients by careful correlation of evidence derived on clinical examination, biochemical studies and liver biopsy.

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EDITORIAL

Bacillary Dysentery

Bacillary dystentery is a form of diarrhea which is accompanied by straining, tenesmus, blood and pus. Two forms of dysentery, bacillary and amebic, are recognized, each of which constitutes an entirely different disease.

Bacillary dysentery is very common in the tropics and it is also found in temperate climates. It may occur in epidemics, especially in closely quartered areas where the hygiene is faulty. When acute enteritis is endemic in children and is associated with the passage of pus and blood, the disease is quite serious and may end fatally. Adults seem to be more likely to develop an immunity.

The bacilli causing dysentery belong to either the Shiga or Flexner group. The Shiga bacillus is a non-mannite fermenter and produces an exotoxin and an endotoxin. The Flexner type ferments mannite and produces no exotoxin. Its endotoxin, however, is much less harmful. By isolating the organism from the feces, its differentiation is determined by means of agglutination test just as is done in typhoid fever.

Usually the disease, in its early stages, is diagnosed as a colitis, although the lower part of the ileum may also be involved. As a result of the action of the toxin produced by the bacilli, an acute inflammation of the bowel wall ensues with deep or superficial clear cut ulcers, in contrast to that found in amebic dysentery. An inflammatory exudate consisting of polymorphonuclear leucocytes and fibrin, together with necrotic material, may form a false membrane and large shreds may be passed in the stools.

The acute infection lasts one to seven weeks or it may become chronic with periodic recurrences. Pus, blood and mucus are present in the stools in large quantities and with all this, the disease is localized without signs of septicemia, or splenic or hepatic involvement. Although multiple liver abscesses may occur at times, they are rather rare. The exotoxins of the Shiga bacillus may cause involvement of the nervous system, such as peripheral neuritis and at times lesions in the gray matter of the cord and the medulla and also painful effusions into the joints.

Treatment with the serum prepared from the Shiga bacillus has been found satisfactory in the acute cases.

Prognosis depends upon early diagnosis and the use of the proper serum.

Samuel Weiss

CHAPTER ACTIVITIES

Boston Chapter

A meeting of the Boston Chapter of the National Gastroenterological Association was held at the Boston City Hospital on Monday evening, 27 April 1953.

The program of the evening consisted of a symposium on "The Patient Who Cannot Eat". Dr. Charles S. Davidson presented "Sugar and Protein Parenteral Feeding" and Dr. Arnold Relman spoke on "Water and Electrolyte Requirements".

New Jersey Chapter

A meeting of the New Jersey Chapter of the National Gastroenterological Association was held on 9 February 1953 at which the scientific session consisted of a seminar on "Gastroenterological Problems in Pediatrics".

At the meeting held on 9 March 1953, a symposium on "Pancreatic Disease" was presented. Dr. David Dreiling spoke on physiologic aspects, Dr. Earl J. Halligan spoke on surgical aspects and Dr. Herbert Greenfield presented various problems.

New York Chapter

The New York Chapter of the National Gastroenterological Association held a meeting on Monday, 13 April 1953. The speakers were Dr. Howard Patterson, Dr. Mark M. Ravitch and Dr. Irving Innerfield.

NEWS NOTES

Ladies Auxiliary Program

The newly organized Ladies Auxiliary of the National Gastroenterological Association, at its first meeting in October of 1952, appointed a committee to arrange social activities for the wives of members and guests attending the Eighteenth Annual Convention of the National Gastroenterological Association.

This committee, under the chairmanship of Mrs. Felix Cunha, San Francisco, Calif., met at the Hotel Roosevelt in New York City on Sunday, 19 April 1953. In addition to Mrs. Cunha, those present included Mrs. Sigurd W. Johnsen, Montclair, N. J., Mrs. Arthur A. Kirchner, Los Angeles, Calif. and Mrs. Samuel Weiss, New York, N. Y.

A tentative program of events is being planned which will include a tour of Los Angeles and its environs, attendance at the convocation ceremony, the President's Annual Reception, the Annual Banquet and a luncheon.

Complete details concerning the activities of the Ladies Auxiliary will be contained in a letter which is to be mailed to all the ladies.

At the meeting in New York City, a Nominating Committee consisting of Mrs. Cunha, Mrs. Weiss and Mrs. Johnsen was appointed to nominate officers for the next year.

Eighteenth Annual Convention

The program for the Eighteenth Annual Convention of the National Gastroenterological Association is in its final stages of preparation. Among the subjects to be covered at the three-day sessions in Los Angeles, California on 12, 13 and 14 October 1953 are: a symposium on "Cirrhosis of the Liver", a panel discussion on "Peptic Ulcer", a panel discussion on "Diagnosis and Management of Diseases of the Large Bowel" and a panel discussion on "Latest Development in Cancer Research".

In addition there will be several individual papers presented.

The full program will be included with the September 1953 issue of The Review of Gastroenterology.

Hotel reservation cards have been mailed to the members of the National Gastroenterological Association. Others may obtain cards by writing to the Executive Officer, National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

Course in Postgraduate Gastroenterology

Application blanks and preliminary announcements for the Fifth Annual Course in Postgraduate Gastroenterology of the National Gastroenterological Association have been mailed to members of the Association.

A distinguished faculty, selected from the medical schools in and around the Los Angeles area, will cooperate with co-chairmen Drs. Owen H. Wangensteen and I. Snapper in presenting this Course.

The fee for the three days is $35.00 for members and $50.00 for non-members. Additional information and enrollment blanks may be obtained from Dept. G.S.R., National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

In Memoriam

We record with profound sorrow the passing of Dr. Joseph S. Diamond, New York, N. Y., Fellow of the National Gastroenterological Association.

We extend our deepest sympathy to the bereaved family.

ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

ESOPHAGEAL HIATUS HERNIA: A. Vanderkloot, J. Am. Geriat. Soc. pp. 138-142 (Feb.), 1953.

This study, made in geriatric patients particularly, arrived at the following conclusions:

1—Hiatus hernia is a common finding on routine gastrointestinal examination but in many cases it does not produce symptoms.

2—The clinical picture of hiatus hernia varies greatly and may resemble that of many other upper abdominal conditions.

3—One symptom that should be stressed is severe hypochromic anemia, often without gastrointestinal symptoms.

4—Except for the rare congenital type, it is particularly a condition found in patients over fifty years of age.

5—The majority of patients will respond to medical management. When necessary, surgical treatment, if properly performed, is usually successful.

J. R. VAN DYNE

STOMACH

CANCER OF THE STOMACH: Henry K. Ranson. Surg. Gynec. & Obst. 96:275-287, (March), 1953.

During the years 1934-1946 inclusive 1,264 patients with gastric cancers were observed and in 457 cases or 36 per cent definitive surgical procedures were carried out. The over-all operative mortality was 18.1 per cent and was highest (40.7 per cent) for proximal resection (esophagocardiectomy) and next highest (22.9 per cent) for total gastrectomy, new procedures which were introduced during this period. From an examination of the autopsy material with reference to residual neoplasm in 55 cases of postoperative death, in only three was there evidence that a total gastrectomy, instead of the subtotal resection performed, might have given a better result. Microscopic examination of these specimens removed at operation revealed metastasis to the original lymph nodes in 70 per cent, microscopic or macroscopic invasion of the perigastric adipose or connective tissue in 33.7 per cent, and involvement of both of these tissues in 23.6 per cent. Follow-up data concerning the 343 cases of operation for cure revealed the following: 28 per cent of the patients survived for five or more years after operation; the males exhibited a slightly higher operative mortality but also a slightly higher five-year survival rate than did females. There was no convincing evidence that the age of patients at the itme of operation affected the prognosis; partial gastrectomy, whether a distal or proximal resection, resulted in approximately the same number of five-year survivals, i.e., nearly 30 per cent. Only 6.7 per cent of patients who survived total gastrectomy survived for five or more years; when involvement of the regional lymph nodes had occurred 16 per cent survived for five or more years, whereas, in the group without nodal involvement there were approximately 50 per cent of five-year survivals. With involvement of the perigastric adipose or connective tissues 16 per cent survived for five years and in the absence of such demonstrable in-

volvement 35 per cent were living at the end of five years. When both of the modes of spread mentioned had occurred, only 8 per cent of the patients survived for five or more years; in the contrasting group when both nodes and adnexal tissues were negative, the five-year survival was approximately 50 per cent. The five-year curability was higher for operations performed during the first half of the study period than for those performed during the more recent years. This latter may have been due to the operations involving multiple procedures which increased the radicalism of attack in the later group. Follow-up studies concerning long survival periods calculated on the basis of the number of patients who could have survived the required number of years revealed that 24.2 per cent lived seven or more years, 18.7 per cent ten years, 19.3 per cent twelve years, 11.8 per cent fifteen or more years. The number of five-year survivals following definitive surgical treatment and based on the total number of patients seen (1,264) was 7.8 per cent.

J. R. Van Dyne

FAILURE OF SURGERY TO RELIEVE SYMPTOMS IN PROLAPSE OF THE GASTRIC MUCOSA THROUGH THE PYLORUS: E. M. Rappaport, A. Alper, and E. Rappaport; Ann. Int. Med., pp. 224-233, (Feb.), 1953.

The authors, in an excellent study, point out that hitherto it was felt that surgery, and in particular pyloroplasty with excision of the extruded antral mucosa, was the best method of treatment for patients who did not benefit from a medical regime. However, such favorable reports seem to have been based on a postoperative follow-up of three months or less, while many of the other patients had recurrent symptomatology. Then too, although hemorrhage has been reported as a common complication of such prolapse, definitive sites of bleeding are rarely discovered in those cases brought to surgery. In the patients reported on in this study it was found too that relief was obtained in 75 per cent of their patients but again, a follow-up for longer than the three month period disclosed a return of symptoms. In addition all of these patients gave histories of even longer periods of remission prior to operation. The poor surgical results can be attributed directly to the fact that the symptoms were unrelated to the extrusion of gastric mucosa into the duodenum. It is interesting to note how great a psychosomatic component was present in these patients and how when the psychic stresses were neutralized, the complaints would disappear. The authors conclude that transpyloric mucosal prolapse is common and rarely a primary cause of symptoms. It would therefore behoove a more careful study of other causes, both organic and functional, before subjecting such patients to surgery. Finally, in cases of repeated upper gastrointestinal hemorrhage which require surgery, when no other abnormality than that of prolapsing gastric mucosa is found, and the cause of hemorrhage not seen even at operation, they recommend a high subtotal resection rather than mere excision of the redundant antral mucosa.

J. R. Van Dyne

INTESTINES

EXPERIMENTAL INTRAPLEURAL SUBSTITUTION OF THE RIGHT COLON FOR THE RESECTED ESOPHAGUS. W. Fry. Surg. Gynec. & Obst. 96:315-322, (March), 1953.

In the dog the right colon is unsatisfactory as a substitute for the esophagus. Its length is too short for total esophagoplasty. Its lumen is too small to permit large boluses of food to pass through to the stomach. The vascular supply of the right colon in the dog is not always dependable after ligation of the right colic and ileocecocolic arteries. However, healing of the anastomosis of colon and esophagus was satisfactory. Peristalsis was seen in the intrathoracic colic segment. Objections to the use of the right colon for esophagoplasty in the dog are not applicable to the right colon in man. An outline of a proposed right colon esophagoplasty in man is presented. The author does not propose that esophagocologastrostomy supplant esophagogastrostomy, which is

currently the operation of choice following most esophageal resections, especially for cancer. However, it may be a preferable operation in certain cases of benign lesions of the esophagus, such as strictures and tracheoesophageal fistula which cannot be adequately treated by primary anastomosis.

J. R. Van Dyne

SURGERY OF THE COLON IN THE GERIATRIC: R. B. Turnbull, Jr. and G. Crile, Jr., J. Am. Geriat. Soc. pp. 132-37, (Feb.), 1953.

There is little risk in operative procedures for cancer of the colon in elderly patients. Three hundred twenty-five resections with three deaths are reported. The modern colon surgeon employs resection with immediate anastomosis whenever possible. This results in low patient morbidity and complications are few as compared with multiple stage exteriorization procedures. The antibiotic drugs can be given much of the credit for lowered mortality and morbidity, since sepsis and its sequelae have practically disappeared as a cause of death. The incidence of phlebitis and pulmonary embolus is decreasing, probably because of antibiotic drugs. Complications of colon cancer, such as obstruction, hemorrhage, or severe anemia make surgery mandatory regardless of age.

J. R. Van Dyne

PANCREAS

LABORATORY PROCEDURES OF USE IN THE DIAGNOSIS OF PANCREATITIS: E. E. Wollaeger. Surg. Gynec. and Obst. 96:371-374, (March), 1953.

By far the most important laboratory procedures for diagnosis during attacks of acute or relapsing pancreatitis are the tests for the concentration of amylase and lipase in the serum. These tests are relatively simple to perform and should be carried out on every patient examined during or soon after an attack of abdominal pain the cause of which is not entirely clear. The determination of serum amylase can be used as an emergency procedure since the results may be available within an hour after blood for the test is drawn. The determination of serum lipase cannot be used for such emergency purposes, since the results do not become available for twenty-four hours after blood is drawn. Following an attack, the concentration of serum amylase usually returns to normal in roughly one to four days while that of serum lipase may remain increased for a longer time. Increased concentration of the serum enzymes is not always found even during proved attacks of pancreatitis. This can sometimes be explained on the basis of such extensive damage to the acinar cells of the pancreas that they are rendered incapable of elaborating the enzymes. Increased concentrations of serum amylase and lipase during painful abdominal seizures are not pathognomonic of pancreatic disease since they may sometimes be found in the presence of acute perforation of a duodenal ulcer, in the presence of peritonitis from other causes, and in intestinal obstruction. Instances have been reported where increases have occurred following the injection of codeine or morphine in patients who had no pancreatic disease but who were apparently sensitive to these drugs. However, with the exceptions of the increases following the injection of opiates (which are rare) and for a very few of those which accompany acute perforation, increases from extra pancreatic causes have not reached the high values usually found in acute attacks of pancreatitis.

Slight increase in the concentration of serum bilirubin giving a direct reaction to the van den Bergh test is a common occurrence in cases having acute episodes of abdominal pain due to pancreatitis. It is therefore often worthwhile to order a determination of serum bilirubin along with a determination of serum enzymes in patients having an attack of abdominal pain of unknown cause. More prolonged increases of serum bilirubin of greater magnitude may occur in patients with chronic pancreatitis in whom a common bile duct has become partially obstructed as a result of inflammation or pseudocyst formation in the head of the pancreas. Transient increases of blood sugar and glycosuria during attacks of abdominal pain may occasionally be the first clue to the diagnosis of pancreatitis and are worth seeking by means of appropriate laboratory procedures. Any patient who has a long standing history of recurring attacks of abdominal pain and in whom diabetes mellitus

develops should be suspected of having chronic relapsing pancreatitis.

Roentgenograph of the region of the pancreas may show calcification in this gland and is diagnostic of chronic pancreatitis. More than a fourth of the patients with chronic relapsing pancreatitis develop steatorrhea due to insufficiency of external pancreatic enzymes. Another procedure which could be of use in the diagnosis of chronic pancreatitis is the analysis of duodenal content after stimulating the flow of pancreatic juice by the intravenous injection of secretin.

J. R. VAN DYNE

PREVENTION OF PANCREATIC FAT NECROSIS: H. L. Popper, and H. Necheles. Surg. Gynec. & Obst. 96:299-300, (March), 1953.

The administration of acridine, cysteine hydrochloride, protamine sulfate, and streptokinase-streptodornase was without effect on the development of fat necrosis. However, the administration intraperitoneally of sodium formaldehyde sulfoxylate lowered the occurrence of fat necrosis from 85 to 38.5 per cent. The authors feel that this favorable result is possibly due to inhibition of trypsin or lipase or of both.

J. R. VAN DYNE

PATHOLOGY AND LABORATORY RESEARCH

IRON METABOLISM: Clinical Evaluation of Iron Stores. A. R. Stevens, Jr., D. H. Coleman, and C. A. Finch. Ann. Int. Med., pp. 199-205, (Feb), 1953.

Iron stores were evaluated by direct examination of particles of aspirated marrow. Hemosiderin iron, when present, represents iron available for hemoglobin production. In the normal individual, small amounts of hemosiderin were visible. A striking difference in marrow iron was found between men and women. In anemias other than those associated with blood loss, there was a shift of iron from the red cells to the tissue stores, which was reflected in an increase in the marrow hemosiderin. In iron deficiency there was a virtual absence of marrow iron. Only those patients with a marked reduction or absence of marrow iron respond to iron therapy. The anemia of infection may be clearly separated from iron deficiency anemia by examination of marrow iron.

J. R. VAN DYNE

BOOK REVIEWS FOR GASTROENTEROLOGISTS

MODERN MEDICAL MONOGRAPHS, CIRCULATORY DYNAMICS, PHYSIOLOGIC STUDIES: Carl J. Wiggers, M.D., Sc.D., F.A.C.P., Professor of Physiology and Director, Department of Physiology, School of Medicine, Western Reserve University, Cleveland, Ohio. 107 pages. Grune and Stratton, New York, N. Y., 1952. Price $4.00

This little monograph consists of the several discourses on experimental aspects of circulatory dynamics as developed by a distinguished and experienced physiologist and noted student of the circulatory system. Many bibliographic references to the literature are included with each of the three chapters.

This is an excellent presentation of several important problems of circulatory dynamics in an easily understandable and instructive manner.

CARDIAC EMERGENCIES AND HEART FAILURE, PREVENTION AND TREATMENT: Arthur M. Master, M.D., Cardiologist, Mt. Sinai Hospital, New York, N. Y., Marvin Moser, M.D., Former Fellow, Cardiology, Mt. Sinai Hospital, New York, N. Y. and Harry L. Jaffe, M.D., Adjunct Physician, Cardiology, Mt. Sinai Hospital, New York, N. Y. 159 pages, illustrated. Lea and Febiger, Philadelphia, Pa., 1952. Price $3.00

This monograph by experts on the subject of cardiac emergencies is one of the best little volumes available. This little monograph should be carefully read by all practicing physicians, internes, residents, medical students, surgeons and clinicians.

The reviewer recommends that all hospital medical libraries should have several copies within easy reach for quick reference.

X-RAY INTERPRETATION: H. Cecil H. Bull, M.A., M.B., M.R.C.P., Honorary Consulting Radiologist to the Royal Waterloo Hospital, London and the General Hospital, Southend-on-sea, with a chapter on Radiography of the Head by James W. D. Bull, M.A., M.B., M.R.C.P., D.M.R., Assistant Radiologist, St. George's Hospital, Radiologist, Maida Nale Hospital for Nervous Diseases, Assistant Radiologist, National Hospitals. Second Edition. 406 pages with 287 original illustrations by the author. Oxford University Press, Geoffrey Cumberlege, London, New York, Toronto, 1951. Price $5.50.

Eighteen years ago, the first edition appeared and now the much improved and uptodate text of the second edition is available to students, x-ray graduate students, residents, internes and young radiologists.

This condensed informative and well written book should be studied by all those interested in x-rays as an aid to clinical diagnosis. It covers many of the more common pathological conditions and some of the more unusual ones.

The normal appearance is emphasized to make it easier to recognize the pathological entities. Simple line drawings and silhouettes are used for illustrations.

BASIC MEDICAL PHYSIOLOGY: W. B. Youmans, Ph.D., M.D., Professor of Physiology, University of Wisconsin, Madison, Wisc. 436 pages. The Year Book Publishers, Inc., Chicago, Ill., 1952. Price $7.50.

The physiologic principles essential for every medical student to prepare him for clinical and pathologic physiology, are clearly, concisely and understandably presented by an experienced teacher of the subject. The endocrine system is contributed by Dr. Joseph B. Trainer.

Of interest to young gastroenterologists and students interested in gastroenterology are chapters 19. 20. 21, 22. 23, 24 and 25 on motility of the digestive tract, secretion and actions of digestive juices, absorption from the digestive tract, nutrition and intermediary metabolism of carbohydrate and of fat vitamins, mineral metabolism, the nervous system and senses, taste, physiologic optics, audition, etc., are instructively discussed.

This work is recommended for use by freshmen and sophomore medical students, nurses and premedical students.

IN COMING ISSUES

Papers presented before the 17th Annual Convention of the National Gastroenterological Association and before the Course in Postgraduate Gastroenterology.

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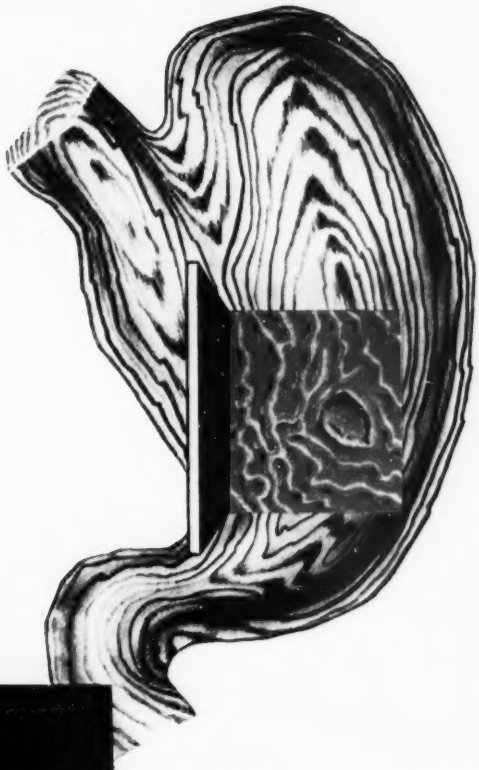

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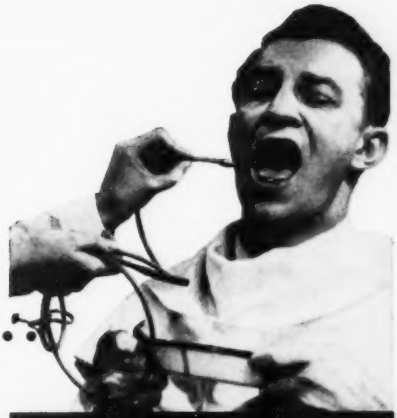

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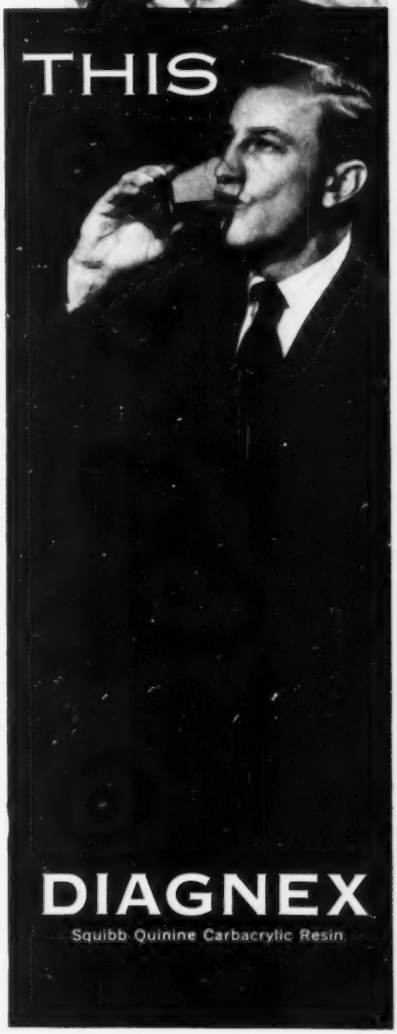

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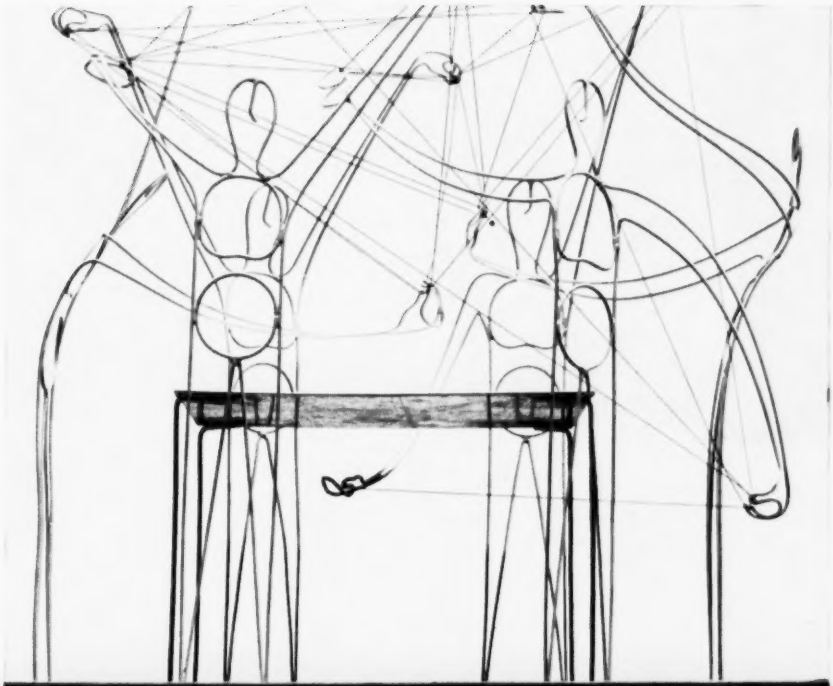

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